VOLUME 41 NUMBER 5

ARCHIVES OF

OPHTHALMOLOGY

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MAY 1949

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $10.00

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago.
Under the Act of Congress of March 3, 1879

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THE SOLUTIONS, AS SOLVED BY EXPERIENCE, INDICATED

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As an example of one method of solving this problem, we have the case of Mrs. H. who required a small distance correction with a +1.50 add for reading. Mrs. H. had no trouble with her bifocals on the street or for reading. It was only when cooking, ironing or washing dishes that she found them unsatisfactory.

The problem was solved to the patient's complete satisfaction by giving her minus add fitovers. These fitovers were made plano in the distance portions and with —0.50 add segments.

The patient was instructed to use the fitovers only when doing house work and to take them off for reading or sewing. She reported, after trying them for several weeks, that in addition to being fine for housework, the fitovers were a big help while playing the piano. She adjusted the music rack slightly farther away and used the distance portion to read the music. The bifocal portion with the aid of the minus add fitovers was focused perfectly for the piano keys.

Minus add fitovers can be used to help quite a wide variety of bifocal wearers. Stenographers, printers, musicians and switchboard operators are often helped by them. In the case of the switchboard operators, it is sometimes necessary to have the upper part a +0.50 sphere and the bifocal a —1.00 add. This gives clear vision all over the board.

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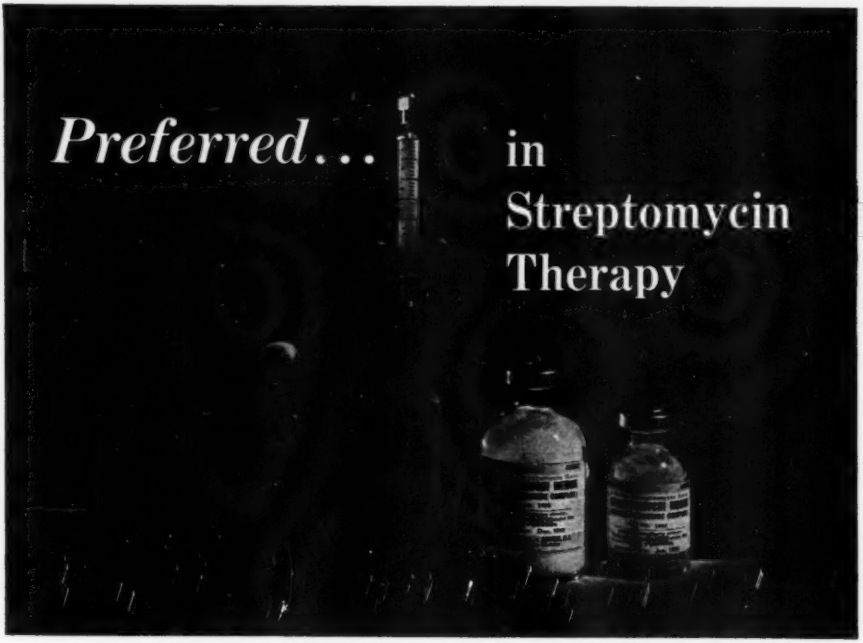

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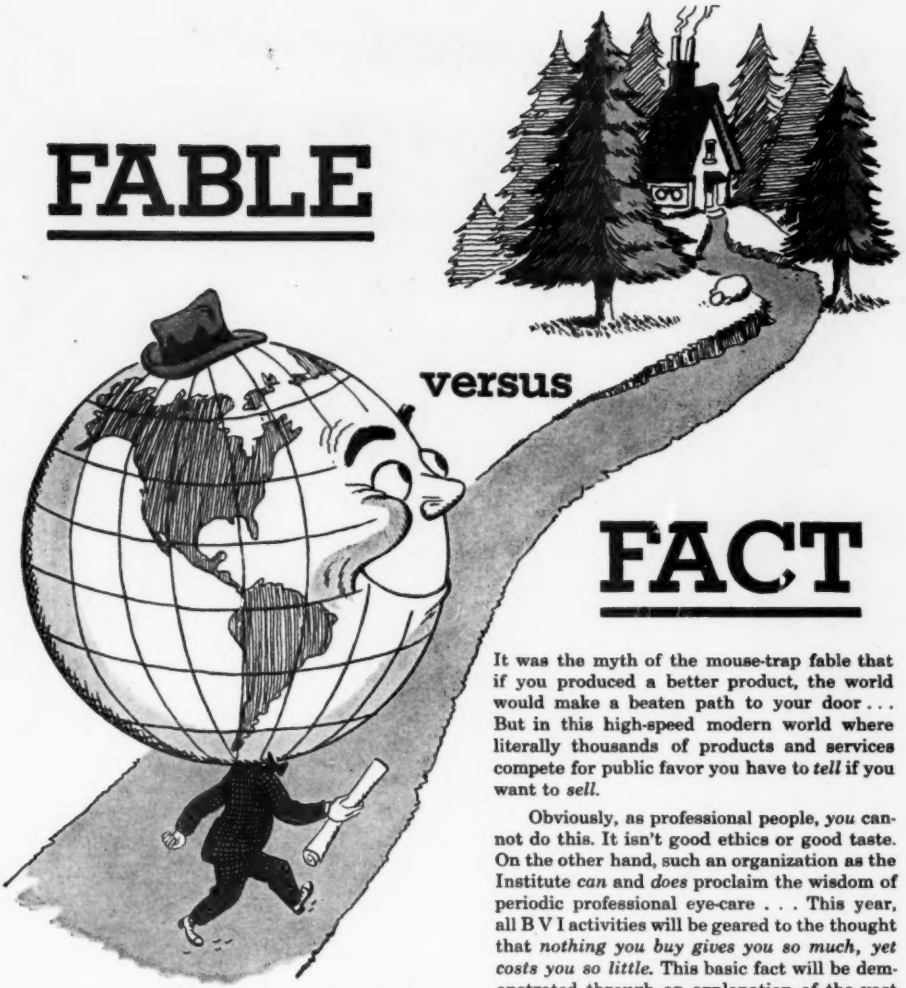

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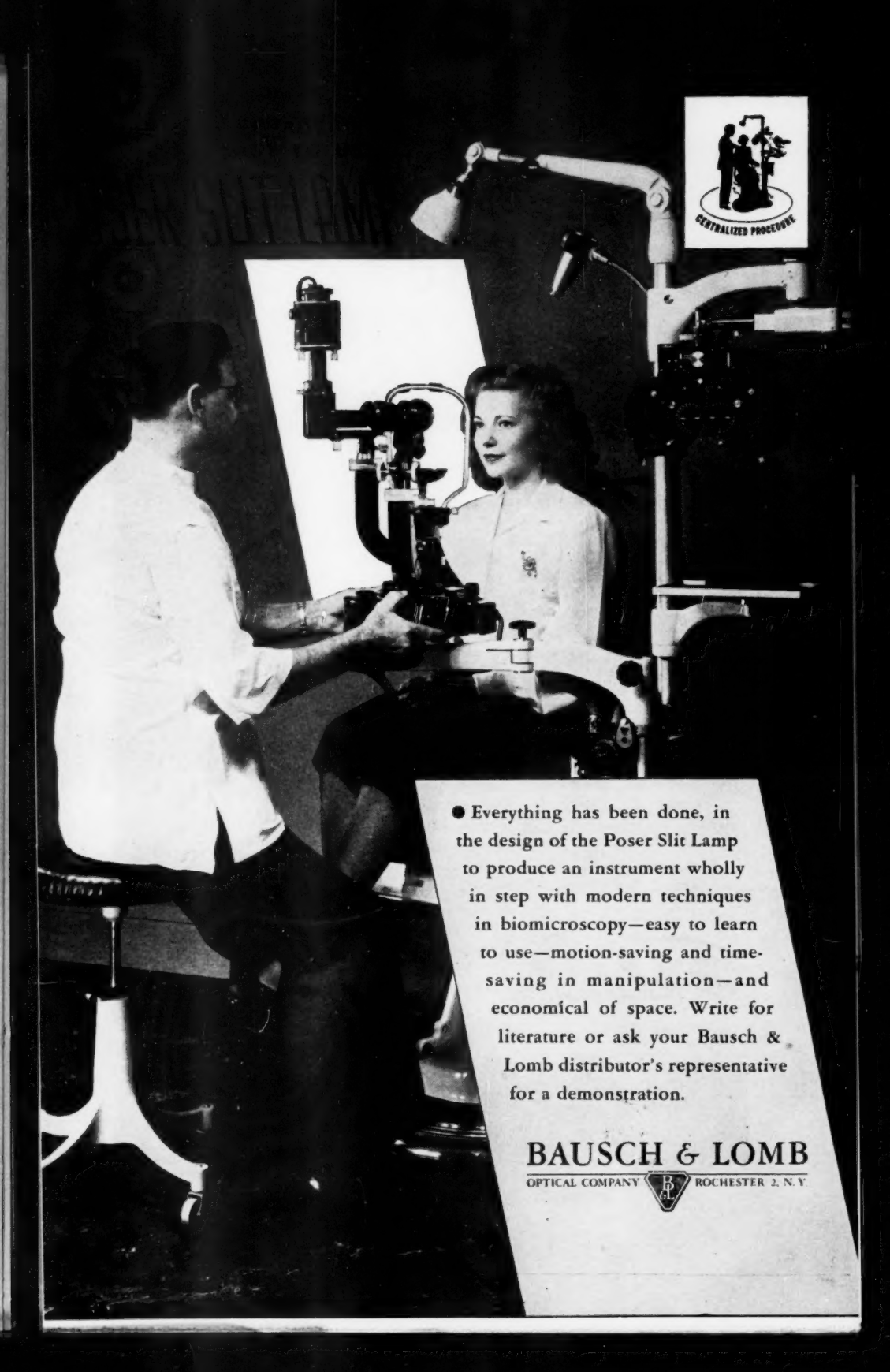
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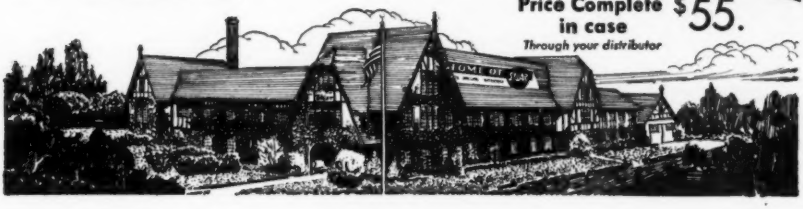

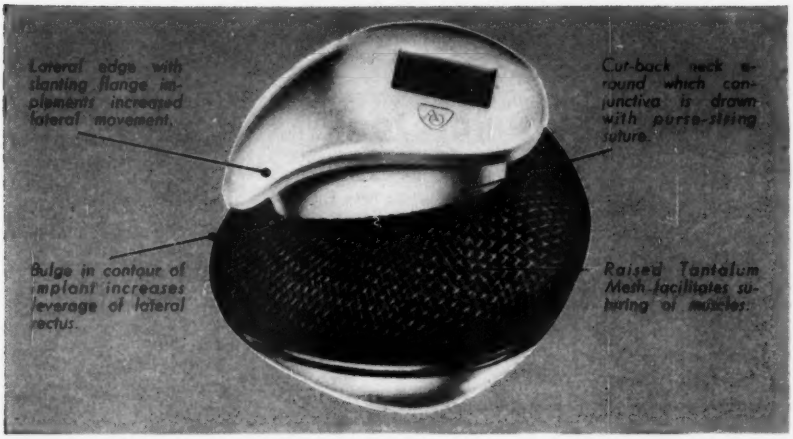
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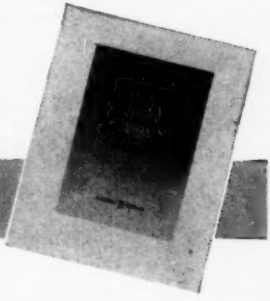

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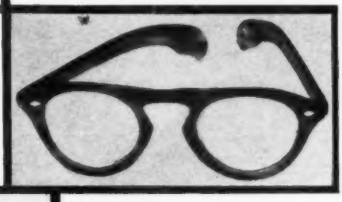

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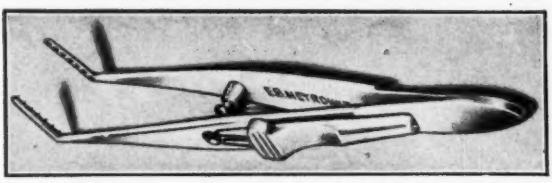

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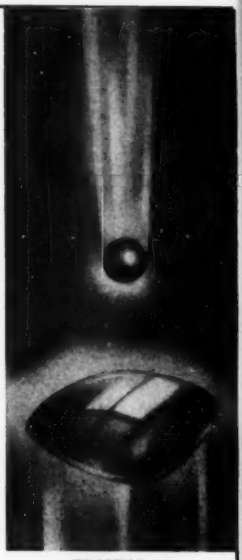

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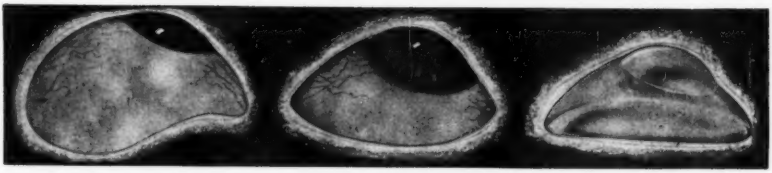

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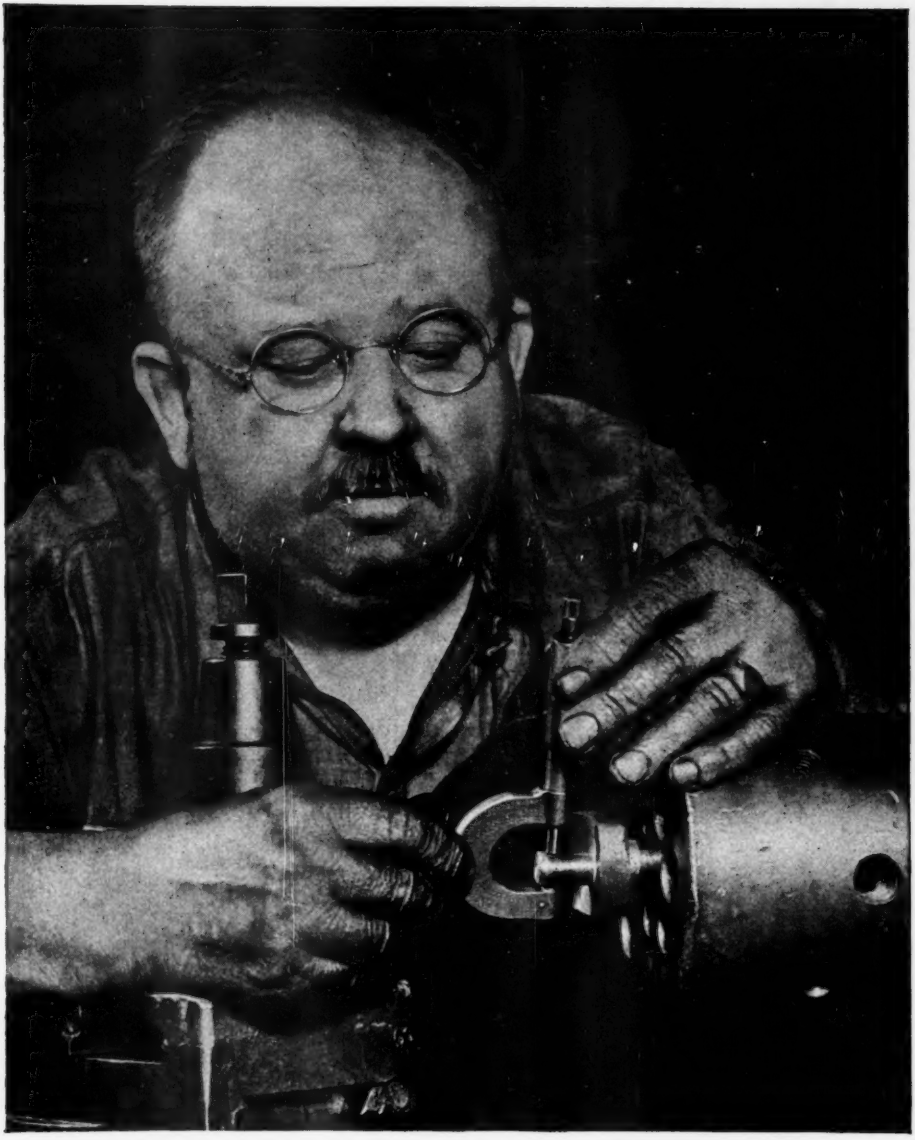

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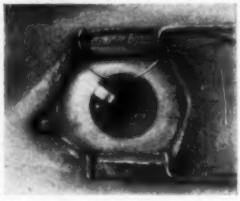

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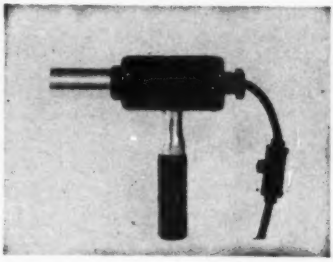

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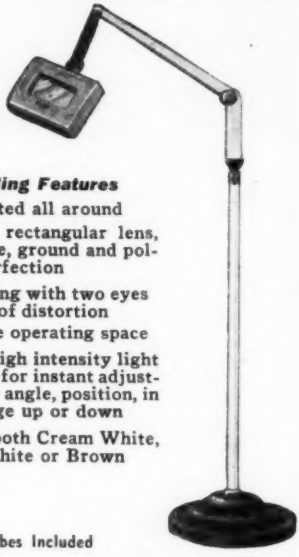

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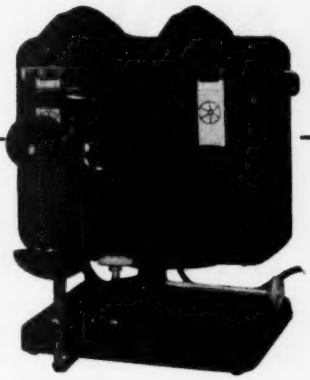

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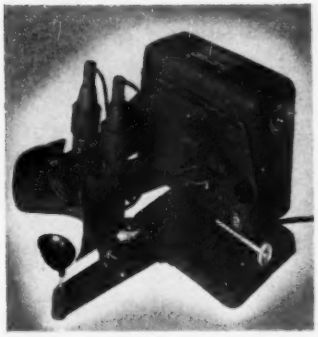

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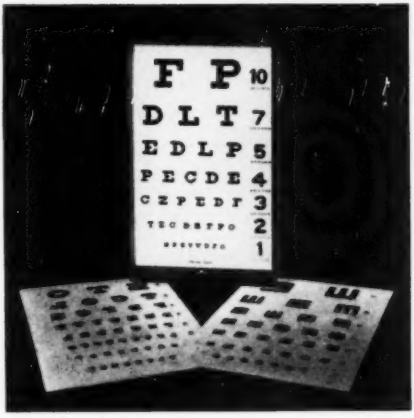

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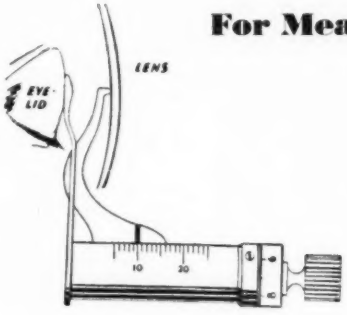

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PERSISTENCE AND HYPERPLASIA OF PRIMARY VITREOUS; RETROLENTAL FIBROPLASIA—TWO ENTITIES

ALGERNON B. REESE, M.D.
NEW YORK

CONSIDERABLE attention has been given to blindness of infants,[1] especially premature infants, due to a condition or conditions called by such various terms as retrolental fibroplasia, persistence and hyperplasia of the primary vitreous, remains of the tunica vasculosa lentis and congenital encephalo-ophthalmic dysplasia. All agree that there has been a large increase in the incidence of this type of blindness.

At the Institute of Ophthalmology, we have seen 202 cases and 128 of these have occurred in the past three years. At the Massachusetts Eye and Ear Infirmary[2] 165 blind preschool children are recorded as residing in Massachusetts, and in 108 of these the blindness is due to retrolental fibroplasia.

As the high incidence of the disease has occurred only in the past ten or more years, and as the disease prior to this period was extremely rare, ophthalmologists over the country have not all incorporated the diagnosis in their repertoire. It is difficult, therefore, to arrive at a true estimate of the incidence of the lesion, because all statistics must be based on reports on the eye from ophthalmologists. The United States Public Health Service[3] has no statistics on the subject. This is also

This work was supported by a donation from Mr. Charles B. Wrightsman.

From the Institute of Ophthalmology of the Presbyterian Hospital in the City of New York.

Read before the Section on Ophthalmology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948.

1. (*a*) Terry, T. L.: Extreme Prematurity and Fibroblastic Overgrowth of Persistent Vascular Sheath Behind Each Crystalline Lens: I. Preliminary Report, Am. J. Ophth. **25**:203-204 (Feb.) 1942; (*b*) Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants: II. Report of Cases, Arch. Ophth. **29**:36-53 (Jan.) 1943; (*c*) Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Infants Born Prematurely: III. Studies in Development and Regression of Hyaloid Artery and Tunica Vasculosa Lentis, Am. J. Ophth. **25**:1409-1423 (Dec.) 1942; (*d*) Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants: IV. Etiologic Factors, Arch. Ophth. **29**:54-65 (Jan.) 1943. (*e*) Reese, A. B., and Payne, F.: Persistence and Hyperplasia of the Primary Vitreous, Am. J. Ophth. **29**:1-19 (Jan.) 1946. (*f*) Krause, A. C.: Congenital Encephalo-Ophthalmic Dysplasia, Arch. Ophth. **36**:387-444 (Oct.) 1946.

2. Personal communication to the author.

3. Personal communication to the author.

true of many state and local organizations concerned with health statistics.

Figures on the incidence of the disease are available in five states. The reports from four of these states are as of April 1947.

The Division for the Blind, Department of Public Welfare, Chicago,[4] reported a total of 109 blind preschool children known in the state, and remarked, "A more adequate coverage of the state would, we feel, reveal considerably more cases." Of this total of 109 children, ophthalmologic reports were available for only 48. For 20 of these 48 children, retrolental fibroplasia was given as the cause of blindness.

The New Jersey State Commission for the Blind [4] reported 96 cases of blindness in preschool children, all of which were covered by ophthalmologic reports, and in 28 of that number retrolental fibroplasia was given as the cause of blindness. Since this report, the New Jersey State Commission has listed a total of 135 cases under their supervision. This rise, within the last nine months, may be real or apparent or both.

The New York State Commission for the Blind [4] reported 115 cases, of which 93 were covered by ophthalmologic reports; 20 of them were cases of retrolental fibroplasia.

The Wisconsin School for the Visually Handicapped [4] reported that 58 visually handicapped preschool children were known to the field service of the Department of Public Instruction, and added, "Information included on causes of blindness is not too reliable, as less than 40 per cent of the cases are based on direct medical reports." Eight of the 58 children had retrolental fibroplasia.

The Division of the Blind, Department of Education of the Commonwealth of Massachusetts [5] reported as of Jan. 1, 1948 that 148 cases of blindness in preschool children were recorded and that in 82 of these a diagnosis of retrolental fibroplasia had been made.

The figures quoted from the Institute of Ophthalmology and from the Massachusetts Eye and Ear Infirmary give too high an incidence of retrolental fibroplasia because both these institutions have manifested particular interest in the disease. The figures available from the four states give too low an incidence of retrolental fibroplasia because many ophthalmologists are not diagnosing this condition, which has only recently assumed importance, and the statistics depend on their certificates. Ophthalmologic reports covering a larger number of preschool children and better case-finding methods of the organizations interested in the blind would lead to the discovery of many more blind preschool children. I feel that a fair estimate is that one third of all cases of blindness in preschool children now are due to retrolental fibroplasia. Further-

4. Lowenfeld, B.: The Blind Preschool Child, New York, American Foundation for the Blind, Inc., 1947, vol. 3, pp. 13-15.

5. Personal communication to the author.

more, there are indications that the incidence has increased not only in the past decade or more, but even more during the past few years.

From a study of our cases, in all of which examination was made with the child under general anesthesia, I believe that at least two different

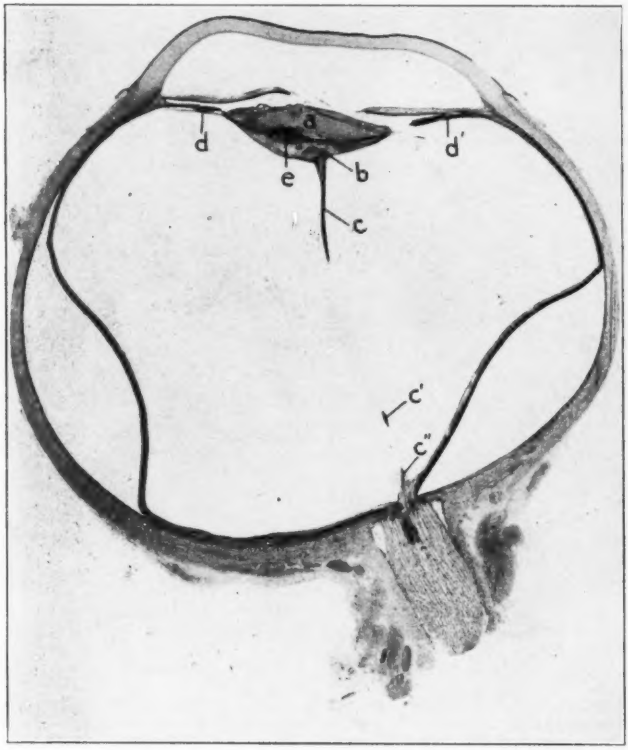

Fig. 1.—Section of an eye of a full term infant with persistence and hyperplasia of the primary vitreous. Back of the lens (*a*) can be seen the fibrous tissue (*b*), extending from which is seen the hyaloid artery (*c*). This artery is also seen at *c'* and at *c"* it is attached to the nasal side of the disk. The long ciliary processes are seen at *d* and *d'*. The posterior capsule of the lens shows a dehiscence at *e*. The retina contains all of its elements, and the detachment is an artefact.

conditions are now being confused. The one will be called "persistence and hyperplasia of the primary vitreous" and the other "retrolental fibroplasia."

PERSISTENCE AND HYPERPLASIA OF PRIMARY VITREOUS

Pathologic Characteristics.—There is adequate pathologic material for study, as this condition is sometimes confused with retinoblastoma and the eye is therefore enucleated.

The histologic picture of this condition (figs 1 and 2) is characterized by the presence of dense fibrous tissue along the posterior surface of the lens, being thickest in the central portion and thinning toward the periphery. It is usually associated with persistence of the hyaloid

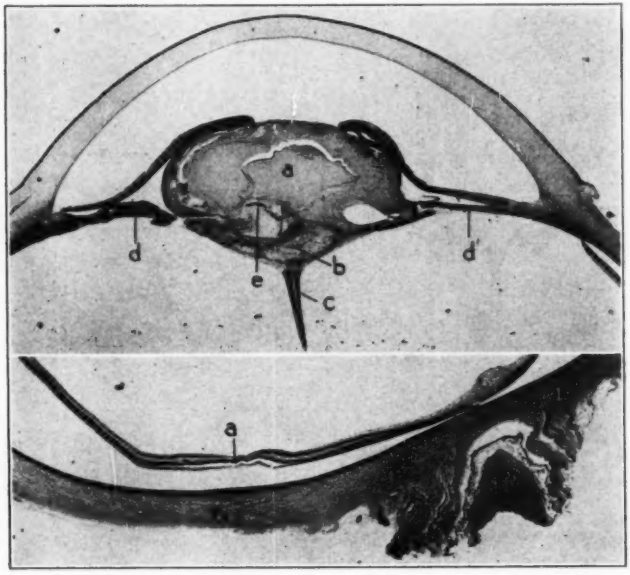

Fig. 2.—Section of an eye of a full term infant with persistent hyperplastic primary vitreous. *A*, back of lens (*a*) is fibrous tissue (*b*), with the hyaloid artery (*c*) attached to it. The long ciliary processes are seen at *d* and *d'*. The posterior capsule of the lens is open at *e*.

B, posterior sector of the same eye, of which *A* is the anterior sector. The retina shows normal structure, with a well formed fovea showing at *a*. The detachment of the retina is an artefact.

artery, which extends to the optic disk. Characteristically, also, the ciliary processes are elongated and extend into the periphery of the fibrous tissue. In some instances the periphery of the retina also extends as a fold far forward, even into the periphery of the tissue. The retina, however, is not detached in the pars optica, and histologically it has all its elements and appears capable of functioning. Sections through the

macular region (fig. 2) show it to be well formed. In this fibrous tissue back of the lens most of the derivatives of mesodermal tissue can in some instances be identified. In addition to connective tissue, smooth muscle, cartilage, fat and blood vessels are sometimes present.

In some cases there is a dehiscence in the posterior capsule of the lens over the site of the fibrous tissue. This may cause a swelling of the lens and, therefore, an advancement of the iris-lens diaphragm so that these structures touch the posterior surface of the cornea (fig. 5), causing a dense corneal opacity, which begins in the central portion and extends to the periphery.

Embryology.—The primary vitreous, which is vascularized mesoderm, is shown in figure 3 *A* at the fourth month of fetal life. Figure

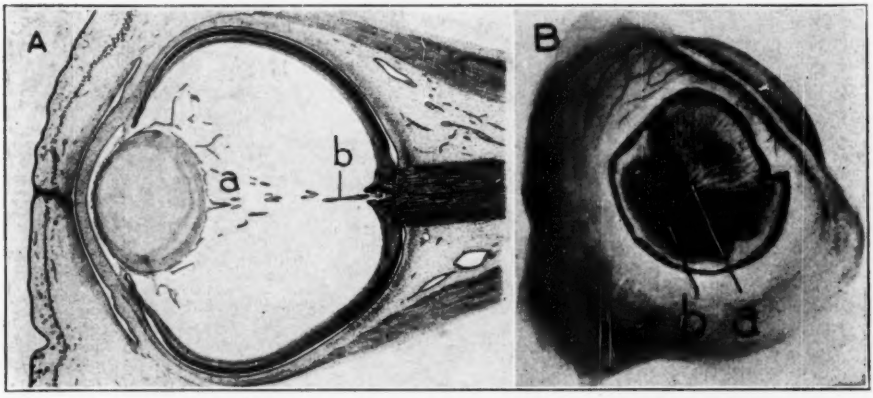

Fig. 3.—*A*, section of normal eye of a 4 month fetus showing the loose vascularized fibrous tissue (*a*) composing the primary vitreous. The hyaloid artery is seen at *b*.

This figure is taken from Bach, L., and Seefelder, R.: Atlas zur Entwicklungsgeschicht des menschlichen Auges, Leipzig, W. Engelmann, 1911-1912.

B, normal eye of 6 month fetus with a scleral window cut out in order that loose vascularized fibrous tissue (*a*) composing the primary vitreous may show. The hyaloid artery is seen at *b*. This specimen was loaned to me by Dr. Henry C. Haden.

3*B* shows the eye of a 6 month fetus with a scleral window cut out so that the primary vitreous is visible. The similarity can be noted between this specimen and that in figure 4, which is the eye of a 6 week old infant with a scleral window cut out so that the persistent hyperplastic primary vitreous can be seen.

Clinical Features.—Clinically, hyperplastic vitreous is seen as dense opaque tissue back of the lens (fig. 5). The tissue has a yellowish to pinkish hue and contains blood vessels, which usually radiate from the

center. The opacity decreases in density around the periphery, where as a result the fundus or the fundus reflex may be seen. The long ciliary processes are usually also visible. Hemorrhage may be seen in the fibrous tissue.

There are lesser degrees of this lesion (figs. 6 and 7), down to its least manifestation, which is the so-called Mittendorf dot.

The condition usually occurs in full term infants who develop normally, and it generally affects only one eye. The affected eye may

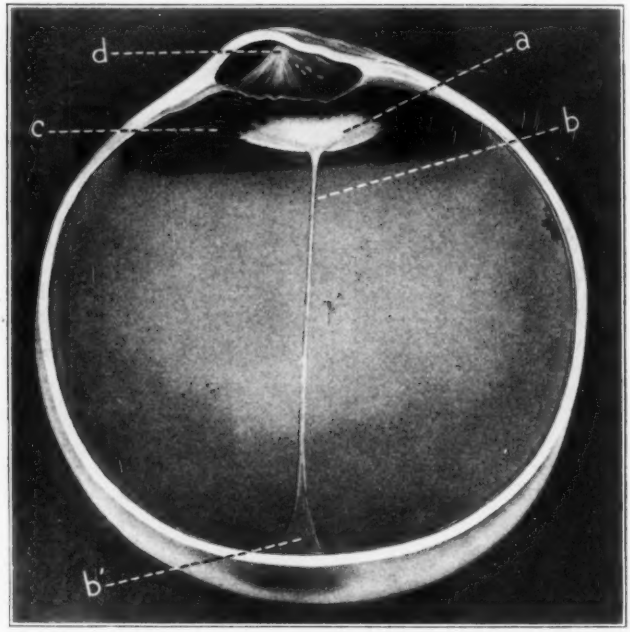

Fig. 4.—Eye of a full term infant with a scleral window cut out to show the persistent hyperplastic primary vitreous. The following features are noted: the fibrous tissue back of the lens, at *a*; the hyaloid artery, at *b* and *b'*, and the long ciliary processes, at *c*. At *d* the iris-lens diaphragm has advanced forward, touching the posterior surface of the cornea and thereby producing a corneal opacity. Sections of the eye showed that this forward extension was due to an opening in the posterior capsule of the lens, which caused a swelling of the lens.

be of the same size as the normal fellow eye, but often it is slightly smaller.

The presence of this lesion is usually detected immediately after birth, so that these patients are seen when they are only a few days to a few weeks old.

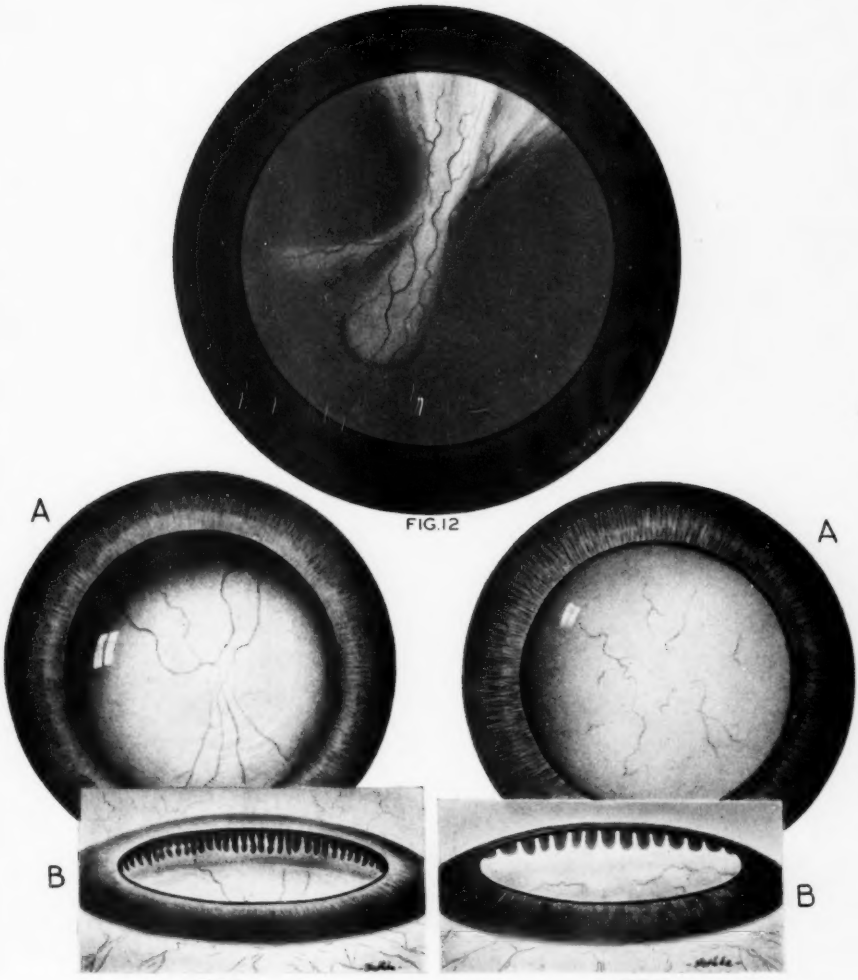

FIG. 12

FIG 5

FIG 11

Fig. 5.—Clinical appearance of persistent hyperplastic primary vitreous. *A*, anterior view; *B*, peripheral view, showing long ciliary processes.

Fig. 11.—Clinical appearance of retrolental fibroplasia in eye of infant born after six and one-half months' gestation. *A*, anterior view; *B*, peripheral view, showing the finger-like projections (dentate processes).

Fig. 12.—Clinical appearance of retrolental fibroplasia in the eye of an infant born after seven months' gestation. The fibrous tissue along with a retinal fold extends from the periphery above toward the equator of the lens, but for the most part it extends posteriorly through the vitreous to the disk, which is drawn inward, giving it a coloboma-like appearance.

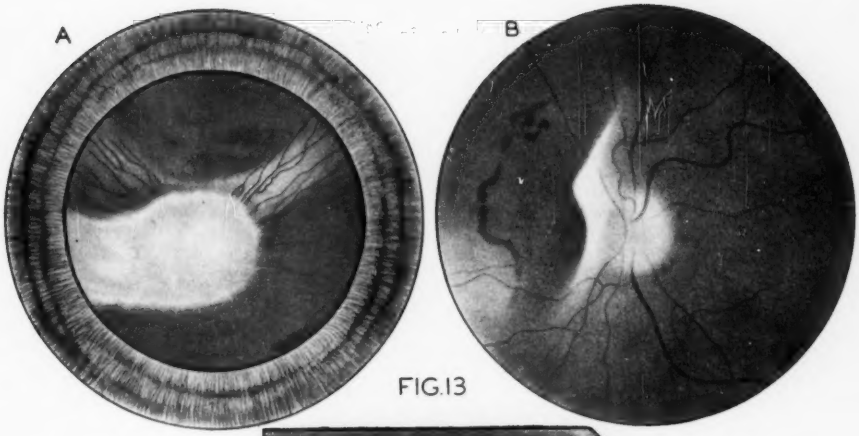

FIG.13

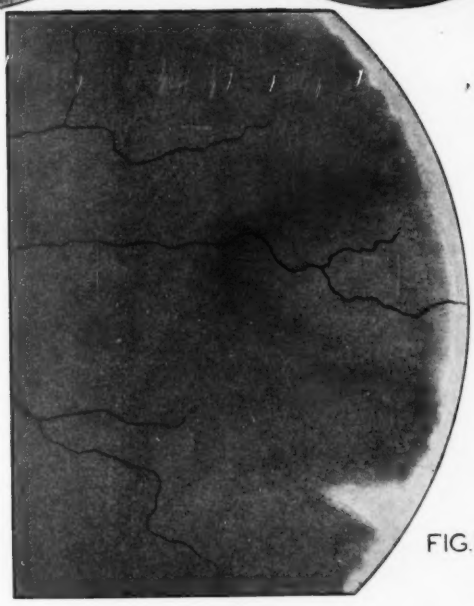

FIG.14

Fig. 13.—Clinical appearance of retrolental fibroplasia in the eye of an infant born after six months' gestation.

A shows tongue of fibrous tissue along with a retinal fold extending from the periphery toward the equator of the lens, but for the most part posteriorly in the vitreous toward the disk.

B, appearance of fundus of the fellow eye, showing the pale, milky appearance, the attenuated vessels, the pigmentary change and the fibrous tissue on the nasal side of the disk. No tissue was seen around the periphery of the lens.

Fig. 14.—Clinical appearance of retrolental fibroplasia in the eye of an infant born after seven months' gestation. Far in the periphery, around the base of the vitreous on the temporal side, can be seen the grayish white fibrous tissue. There is a small, flat detachment of the retina. A similar lesion was present in the fellow eye.

There can be no doubt that the lesion is congenital. The fibrous tissue back of the lens has the pyramidal shape of the primary vitreous and is observed at birth or shortly thereafter. As this tissue has no connection with the ciliary body it could not be situated where it is as the result of an acquired lesion. If it were an acquired lesion, there would of necessity be some connection between the tissue and the surrounding ciliary body or the peripheral portion of the retina. Furthermore, the fact that the hyaloid artery is almost constantly present points to the congenital nature of the lesion.

Moreover, the tissue back of the lens is thickest in the central portion and thinnest at the periphery; were it acquired from the surround-

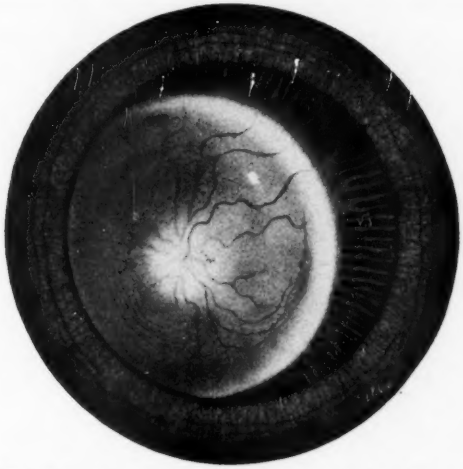

Fig. 6.—Clinical appearance of a persistent hyperplastic primary vitreous of a lesser degree than that shown in figure 5.

ing vascular structures of the ciliary body, choroid or retina, the peripheral portion would be the thicker. The fibrous tissue sometimes contains cartilage and all other mesodermal elements, and it is obvious that these are not present as a result of changes in acquired organized fibrous tissue.

Eyes with hyperplastic vitreous are sometimes enucleated with the clinical diagnosis of retinoblastoma, not only because of a similar clinical appearance but also because the lesion appears unilaterally at birth in full term infants. It is important to make the correct differential diagnosis and thus avoid unnecessary enucleation, for an eye with hyperplastic vitreous has the potentiality of vision. Even the fovea

appears intact. Theoretically, one should be able to remove the opaque tissue back of the lens and obtain a functioning eye. The treatment will be discussed later.

RETROLENTAL FIBROPLASIA

Pathologic Features.—There is a scarcity of good pathologic material for study of this condition, as the clinical appearance does not

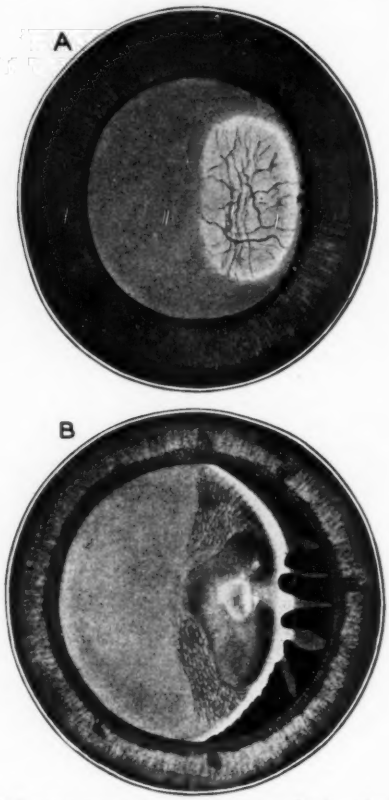

Fig. 7.—Clinical appearance of persistent hyperplastic primary vitreous of a lesser degree than that shown in figure 6.

A, appearance of lesion when patient was 9 days old; *B*, appearance of the same lesion when the patient was 7½ years old.

closely simulate retinoblastoma, and the other associated factors, such as prematurity and microphthalmos, help in making the correct diagnosis. The eye, therefore, is seldom enucleated unless there is an

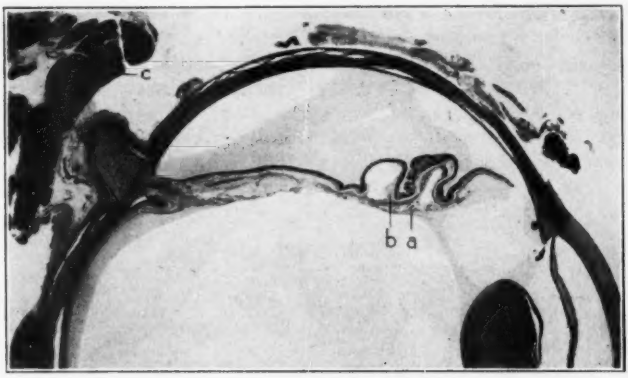

Fig. 8.—Section showing retrolental fibroplasia in an eye of an infant born after six months' gestation (see text for history). Along the surface of the retina, particularly near the ora serrata, is vascularized fibrous tissue (*a*), in which is some hemorrhage (*b*). The contraction of the organized fibrous tissue has caused a detachment of the retina and traction on the optic nerve head. Some strands of fibrous tissue extend from the hemangiomatous tissue to the posterior surface of the lens. A hemangioma which was responsible for exophthalmos during life is seen in the orbit at *c*. The fellow eye showed a similar lesion of hemangiomatous tissue along the surface of the retina, particularly in the periphery.

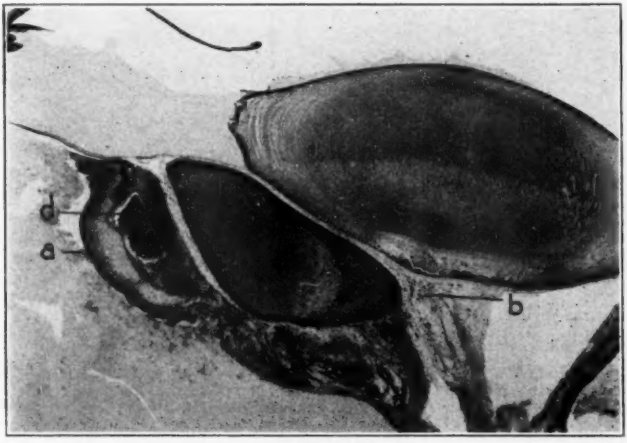

Fig. 9.—Section showing retrolental fibroplasia in an eye of an infant born after six and one-half months of gestation. Over the surface of the detached retina (*a*), near the ora serrata, is a great deal of vascularized fibrous tissue (*b*) with hemorrhage (*c*) and organization (*d*).

advanced pathologic condition, with complete retinal detachment and secondary glaucoma. Then the true picture is masked. We have available for microscopic study 3 globes showing the lesion in a relatively early stage. In addition, I have studied all the material available at the Army Institute of Pathology, and Dr. Bertha Klien has permitted me to study her excellent material.

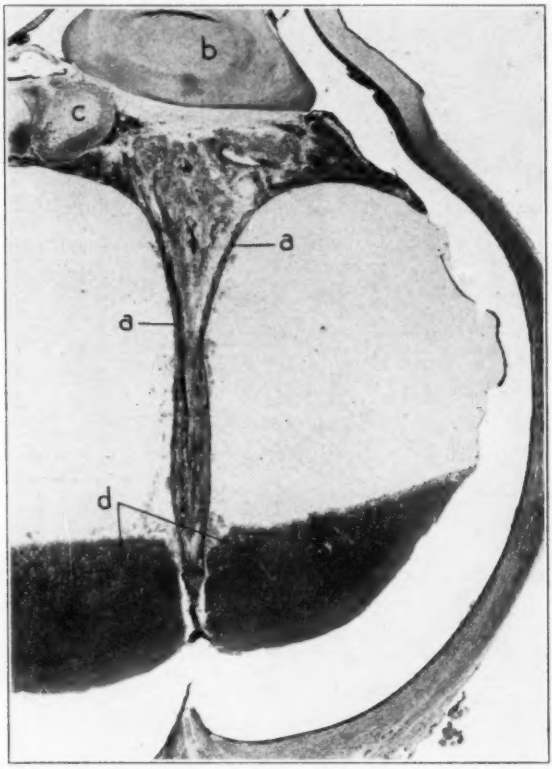

Fig. 10.—Section showing retrolental fibroplasia in an eye of an infant born after seven and one-half months' gestation. Between the completely detached retina (*a* and *a'*) and the lens (*b*) is a vascularized fibrous tissue showing hemorrhage and organization. A blood cyst is seen at *c* and subretinal hemorrhage at *d*.

The pathologic process (figs. 8, 9 and 10) is centered around the base of the vitreous. Here is found fibrous tissue rather rich in vascular channels. This tissue probably undergoes some hyperplasia, but its increase seems to stem mostly from hemorrhage and organization.

The resultant contraction leads to detachment of the retina, which seems invariably to be present. The fibrous tissue extends over the posterior surface of the lens, but for the most part it courses posteriorly into the vitreous in the direction of the disk. In the more advanced stages, the retina is completely detached, and there are old and recent hemorrhages in all stages of organization. Particular attention is called to the case illustrated in figure 8. This case furnishes the earliest microscopic changes in retrolental fibroplasia and seems to give a good indication of the nature of the early changes in this disease.[6]

The history is as follows: Of twins born three months prematurely, one lived and no abnormalities were noted except for typical retrolental fibroplasia in both eyes. The other twin, who weighed 1 pound 10 ounces (737 Gm.) at birth, showed, when several weeks old, an exophthalmos of the right eye. Examination of the fundi was not done with the patient under general anesthesia. After many attacks of cyanosis with cessation of respiration, the infant died, and an autopsy was performed.

The autopsy observations were as follows: hemangiomas of the pharynx, right carotid body and right orbit, both retinas and the adjacent vitreous and the choroid plexus of the fourth ventricle; extramedullary blood formation in the spleen, liver, adrenal glands, kidneys and lymph nodes; splenomegaly; lobular pneumonia of the lower lobe of the right lung; accessory adrenal gland attached to the fallopian tube, and patent foramen ovale.

Microscopic examination of the eyes showed the following changes:

Right Eye (fig. 8): The retina was detached over one-half the globe, and over the retinal surface, particularly the portion detached, there were many blood vessels with a moderate amount of supporting tissue. There was some vitreous hemorrhage, which apparently came from the angiomatous tissue along the surface of the retina. The hemorrhage had become partially organized, and the contraction of this tissue had led to detachment of the retina. At no point could excessive blood channels be seen in the fiber layer of the retina. Behind the globe there was a large nonencapsulated hemangioma containing large blood-filled sinuses surrounded by hyperplastic endothelial cells.

Left Eye: The retina was in position, but along its entire surface were small blood vessels, occurring either as a thin layer or as localized clumps, with relatively little supporting tissue. In places these blood vessels over the retina lay along the surface of the internal limiting membrane, while elsewhere they appeared in the nerve fiber layer.

(This case was cited in a previous article [Reese and Payne [1e]]).

Embryology.—On the basis of the available pathologic material and the clinical characteristics, it is probable that the basic lesion in this condition is the persistence of some of the vascular primary vitreous in the region of the base of the vitreous. In the microscopic sections showing the earlier phases of the disease, this vascularized mesoderm can clearly be seen, and even resembles angiomatous tissue in some

6. This eye was obtained for microscopic examination because the patient, who was one of twins, died at the age of 3 months. The twin of the patient lived and has typical retrolental fibroplasia in each eye.

instances. This tissue does not seem to be in the retina but is definitely internal to the retina. It is from this vascular tissue that the hemorrhages and subsequent organization and contraction stem.

It must be assumed that an important embryologic feature of this condition is the adherence of this persistent vitreous to the adjacent inner layer of the optic cup. Over this layer the secondary vitreous fails to form, and therefore the retina is detached. The subsequent hemorrhage, organization and contraction lead to further retinal detachment.

Clinical Features.—All the clinical observations on which this paper is based were made on patients after the parents had suspected that something was wrong with the infants' eyes. They were made, therefore, on patients from 2 months of age on, and none from birth.

The lesion presents itself in various degrees of development, and this gives a wide range to its clinical manifestations. The condition usually manifests itself (fig. 11) as gray, opaque to translucent, tissue in the anterior portion of the vitreous and back of the lens. The lesion is somewhat vascularized and frequently shows hemorrhage or its sequelae, such as hemosiderosis, giving a greenish tint. The tissue is thickest and most opaque around the periphery in the region of the equator of the lens, especially on the temporal side and above.

Far in the periphery of the opaque tissue, serrations are frequently seen (fig. 11 *B*). These seem to be due in some instances to dentate processes of the opaque tissue, but in other instances the appearance is given by the ciliary processes, which are visible. In the first instance the serrations are the actual finger-like projections of the opaque tissue, whereas in the second instance serrations appear only as such between the valleys of the ciliary processes. It is my feeling that in cases of hyperplastic vitreous the actual ciliary processes are usually seen, whereas in the cases of fibroplasia it is the dentate processes that are usually seen.

The lesion may manifest itself primarily as a peninsula of opaque tissue in the periphery, especially temporally and above (figs. 12 and 13). This tissue radiates out over the posterior surface of the lens in part, but mostly it extends backward into the vitreous toward the optic disk. In the tissue there may be blood vessels, and in rare instances the number and character suggest an angiomatous element. Hemorrhage may be noted in the tissue. There is retinal detachment, the degree of which varies, but usually it manifests itself as a retinal fold confined chiefly to the quadrant in which the opaque tissue is seen. This retinal fold extends from the tissue toward the disk. Sometimes the opaque tissue obscures the underlying detachment. The disk is drawn out toward the detachment, giving it a colobomatous appearance with abnormally arranged blood vessels.

This manifestation of retrolental fibroplasia is certainly the same condition as that spoken of in the literature as congenital retinal fold, congenital falciform retinal fold or ablatio falciformis congenita. Guerry [7] stated that in cases of congenital retinal folds some authors have reported that the hyaloid artery, either the principal trunk or one of the vasae hyaloideae propriae, was attached to the fold or embedded firmly in its substance.

In the lesser manifestations of this lesion (fig. 14) it may be difficult to see the tissue around the base of the vitreous and the equator of the lens. In such cases it is absolutely necessary that one examine the patient while under general anesthesia, using a speculum to retract the lids and forceps to rotate the eye so that the most extreme portion of the periphery can be inspected. It is necessary sometimes to augment these measures by grasping the conjunctiva about 7 mm. from the limbus and pushing the sclera inward at the same time that the globe is rotated outward. In this manner a peripheral view can be obtained even as far as, or beyond, the ora serrata. The lesion is more frequently located temporally, and this is the area more accessible to indentation by the sclera.

A shallow anterior chamber is invariably present. This may become increasingly shallow, so that ultimately not only glaucoma ensues but the iris and lens are in apposition to the posterior corneal surface, particularly in the central area, and thus edema and an opacity of the cornea develop.

Glaucoma was present in about one third of the cases of retrolental fibroplasia. It is difficult, however, to establish definitely the presence of glaucoma, particularly if the tonometric reading is the sole criterion. I feel that the readings of the tonometer are not absolutely reliable in all cases, owing to the fact that the foot plate of tonometers is designed for corneas of adult size and the corneas of eyes with this condition show variations in size and curvature. The Souter tonometer should be the most reliable one to use. Digital palpation should also be reckoned in the final estimate. It is surprising, however, how well these eyes tolerate an increase in the intraocular pressure without showing ectasia of the globe. Some eyes seem to withstand an increase in intraocular pressure for an indeterminate time without developing buphthalmos. The cause of the glaucoma seems to be connected with the extremely shallow anterior chamber but malformation of the filtration angle is probably also a factor.

Eyes with fibroplasia are usually somewhat microphthalmic, but frequently they have a corneal diameter of 10 mm. or more and appear

7. Guerry, DuP., III: Congenital Retinal Folds, Am. J. Ophth. **27**:1132-1135 (Oct.) 1944.

to be of about normal size for the age of the child. After glaucoma has persisted for some time, buphthalmos develops.

Atrophy of the iris, posterior synechias and the sequelae of exudate in the pupil and over the iris may be present. In some of the cases a pupillary membrane of a congenital nature, arising from the collarette of the iris, is present.

Fibroplasia usually affects both eyes and is of about the same degree and type in the two eyes. Occasionally the lesion is of a rather pronounced degree in one eye with the fellow eye showing a lesser degree, or even no opaque tissue, but an abnormal-appearing fundus (fig. 13). In all cases whenever the fundus is visible, it shows definite changes. These changes, which are of a pale, rather milky color, consist of slight, diffuse pepper pigmentation, which occasionally is marked and more or less localized; attenuated blood vessels, especially the arterioles, which are seen as mere threads; white sheathing of some vessels, especially the veins, and mild colobomatous changes of the disk, where the blood vessels show abnormal arrangement.

The lesion is characteristically seen in premature infants but may occur in full term infants. Thirteen of our cases were of full term infants. The incidence is higher in premature infants with the lower birth weights, especially 2,000 Gm. or less. Mental retardation and lack of normal physical development may occur. Nystagmus and microcephaly are sometimes present. The condition occurs in one or more of twins or triplets in from 10 to 15 per cent of cases.

There is no doubt that the lesion progresses after birth. Terry [1a,b] mentioned cases in which he observed the eyes shortly after birth, at which time he could not see anything abnormal in the media or the fundus, but later typical retrolental tissue appeared. This observation has been confirmed and amplified by Owens and Owens [8] and, later, by Unsworth.[9] I have seen numbers of cases in which the fibroplasia was so slight that the fundus could be well seen, only to have the view of the interior of the eye completely obscured later by the increase in extent and density of the retrolental tissue.

Retrolental fibroplasia is usually not noted until about the third to the fifth month after birth. I believe, however, that in all instances at least the matrix of the lesion is present at birth. This is seen around the equator of the lens and at the base of the vitreous. The basic congenital lesion is the remains of some angiomatous mesoderm from the primary vitreous, and from this tissue hemorrhage occurs, resulting in organization and retinal detachment, with perhaps an element

8. Owens, W. C., and Owens, E. U.: Retrolental Fibroplasia in Premature Infants, Tr. Am. Acad. Ophth. (1947) **53**:18 (Sept.-Oct.) 1948.

9. Unsworth: Personal communication to the author.

of hyperplasia. Ultimately, these factors lead to a completely detached retina, which is pulled by contracting fibrous tissue across the anterior portion of the vitreous. Clinically, therefore, the fibrous tissue is viewed just back of the lens and the detached retina lies back of this and sometimes can be seen through the interstices of the fibrous tissue. If the eye, with the patient under general anesthesia, is moved backward and forward with forceps, different levels of opacity in and back of the lens can often be appreciated by parallax. An opacity in the lens will move with the eye; opaque tissue just back of the lens will move against the eye; still another opaque tissue farther back of the lens will move more rapidly against the eye than the more anterior tissue.

I do not believe one can say that the matrix of this lesion is not present at birth without examining the patient while under general anesthesia, and with dilated pupils, using a speculum to retract the lids and forceps to rotate the eye so that the extreme periphery of the fundus may be inspected. Under the best of conditions there is still 4 mm. of fundus in the adult eye which is not accessible to view with the direct ophthalmoscope. In a newborn baby, even under the ideal conditions stated, I doubt whether it is possible to obtain a view beyond the equator of the globe, certainly not this far, without general anesthesia. Inductions of general anesthesia in a newborn premature infant is not feasible, but we hope to develop a method of heavy sedation which will permit an adequate examination. It seems to me that those who believe that the lesion is acquired must give sufficient proof that at least the matrix of the lesion is not present far in the periphery of the fundus, a condition which is indicated by all available pathologic material, as well as by the clinical manifestations.

There is still other evidence that retrolental fibroplasia is essentially a congenital lesion than that afforded by the pathologic material and the clinical behavior. The affected eyes are usually somewhat microphthalmic, and they frequently show a pupillary membrane arising from the collarette of the iris. Sometimes congenital anomalies are present elsewhere and there is an increased incidence of hemangioma of the skin, which is certainly a congenital lesion.

Sometimes the lesion regresses sufficiently to permit a view of the fundus in a case in which previously not even a fundus reflex had been visible. In the few instances in which this has occurred the retina was detached but did not show any angiomatous changes. The explanation for this regression is not clear. It may be predicated on absorption of the hemorrhagic element.

A feature of retrolental fibroplasia which should be mentioned is the high incidence of hemangioma of the skin in the affected patients. A hemangioma of some degree was noted in approximately 25 per

cent of the cases. By the term "hemangioma" I mean not telangiectasis but an actual elevated, and sometimes pedunculated, tumor. The lesions may be extensive and multiple. They may be located in or under the skin anywhere over the body. They are present at birth, and they may enlarge and then regress. This process of involution is interesting and manifests itself as a steady shrinkage in the size of the lesion with wrinkling of the overlying skin. It is due apparently to a spontaneous sclerosis, which is seen first in the central portion of the lesion.

In the Hemangioma Clinic of Memorial Hospital for the Treatment of Cancer and Allied Diseases,[10] 56 mothers of infants and young children having cutaneous hemangiomas were interviewed. An attempt was made to establish any relation of the vascular abnormality in these infants to prematurity, to evidence of maternal infection during pregnancy or to retrolental fibroplasia. No such connection could be determined. Hess, Mohr and Bartelme [11] found hemangiomas of the skin in 8 of 250 prematurely born children, or in 3.2 per cent. They found hemangiomas of the skin in 2 of 156 full term siblings, or in 1.3 per cent. This difference in the incidence of hemangioma in premature and in full term infants does not seem significant, but the incidence of hemangiomas of the skin in premature infants with retrolental fibroplasia is definitely higher than in premature infants in general.

Another feature of interest, and probably of significance, is the fact that the mothers of these children gave a history of vaginal bleeding during pregnancy in approximately 30 to 35 per cent of the cases. In some instances the bleeding warranted hospitalization. Sometimes it was frequent throughout pregnancy, and sometimes it preceded the precipitous birth.

Etiologic Factors.—One can only speculate on possible causative factors. I think the lesion is essentially congenital, and therefore I look to the mother as the medium. Those who believe the lesion to be acquired naturally view the postnatal period of the infant with suspicion.

There is some evidence indicating that the disease may result from a maternal infection of some nature. In support of this it can be said that the incidence of the disease seems to vary in different localities. The incidence of retrolental fibroplasia during the last eight years has been found to average 18 per cent of all premature births in one Boston hospital,[2] while in some other localities the incidence seems lower. My colleagues in other countries, including France, Austria

10. Unpublished data.

11. Hess, J. H.; Mohr, G. J., and Bartelme, P. F.: The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934.

and Australia, tell me that they do not encounter the condition except in a rare, sporadic case. Furthermore, in the fundi of the patients there are clinical manifestations over the areas accessible to examination which indicate that choroiditis of a mild nature has existed. This manifests itself as a diffuse, mild pigmentary disturbance. Some of the eyes having retrolental fibroplasia show evidence also of iridocyclitis. This manifests itself as posterior synechias, atrophy of the iris and the sequela of exudate around the pupillary margin of the iris. Moreover, in the mothers of these patients there is the high incidence of vaginal bleeding during pregnancy, and in some, the evidence of systemic infection of some kind during pregnancy. The latter may consist in a history of fever or of intercurrent infection, such as brucellosis, rubella or ulcerative colitis.

Instances of mild clinical, or even subclinical, infections of the mother affecting the offspring are known to exist. Toxoplasmosis is a subclinical infection of the mother which produces in the offspring chorioretinitis, as well as congenital anomalies. Roentgenograms of the skull in 12 of our cases of retrolental fibroplasia revealed in 1 case a punctate calcification in the brain identical with that seen in toxoplasmosis. Measles, and perhaps other virus diseases, in the mother can produce abnormalities in the offspring. The mother of 1 of our patients had rubella about the second month of pregnancy. There must still be other clinical and subclinical infections of the mother which act in similar fashion. It seems reasonable, therefore, to postulate that in retrolental fibroplasia a maternal infection of some nature is responsible for the variations in the incidence in different localities, for the vaginal bleeding, and thus the premature birth, and for the signs of inflammation such as chorioretinitis and iridocyclitis, in the eyes of the offspring. As pediatricians now save premature infants which would previously have been lost the sequela of this maternal infection in the infant now manifests itself as an increased incidence of a lesion which formerly appeared only sporadically. The increased incidence might also be attributed, in part at least, to an increase in the prevalence of some maternal infection.

Warkany and Schraffenberger [12] produced retrolental fibrous tissue and other congenital anomalies in the offspring of rats by feeding the mothers a diet lacking vitamin A.

The fact that premature infants have anemia, sometimes rather severe, for about the first three months may be significant.

Two features of the condition suggest that prematurity per se is important. These are the relatively high incidence of retrolental fibroplasia in twins and triplets and the not infrequent association of the

12. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Vitamin A Deficiency, Arch. Ophth. **35**:150-169 (Feb.) 1946.

condition with toxemia of pregnancy. Both these factors predispose to premature birth.

COMMENT

As hyperplasia of the vitreous and retrolental fibroplasia are similar clinically, and as the clinical differential diagnosis of the two is seldom confirmed by microscopic examination, it is impossible to state the correct incidence. In our series I estimate that approximately over 90 per cent of the cases were of fibroplasia. I doubt whether the incidence of hyperplasia of the vitreous has changed over the course of years, but I am sure there has been a tremendous increase in the incidence of retrolental fibroplasia in the past decade or more. This may be due entirely or in part to the fact that pediatricians are saving premature infants who formerly would have been lost. Another factor may be an increased incidence of severe maternal infection, which is also responsible for the precipitous birth.

I believe that both these conditions have been confused in the past, that neither is a new manifestation and that both have always appeared sporadically and have been reported in the literature under various names. Hyperplasia of the vitreous [13] has been given various names, such as persistent thickened hyaloid artery with secondary changes (Nettleship, 1873), persistence and thickening of the posterior fibrovascular sheath of the lens (Collins, 1892; Pollock, 1923), atypical development of the anterior part of the vitreous with or without a persistent hyaloid artery (Collins, 1892), congenital membrane behind the lens (Parsons, 1902), persistence of remains of the tunica vasculosa lentis (Brückner, 1907), persistent posterior fibrovascular sheath of the lens (Lane, 1919), persistence of the embryonic fibrovascular sheath of the crystalline lens (Lent and Lyon, 1922), remains of the tunica vasculosa lentis (Gifford and Latta, 1923; Lloyd, 1931) and pseudophakia fibrosa of Czermak (Fuchs, 1923). I think that fibroplasia has been

13. Nettleship, E.: Vascular Cord Traversing Vitreous and Coexisting with Great Plastic Inflammation of Hyaloid, Roy. London Ophth. Hosp. Rep. **7**:632-637, 1873. Collins, E. T.: Pseudo-Glioma, Ophth. Hosp. Rep., London **13**:361-394, 1890-1892. Pollock, W. B. I.: Case of Pseudoglioma Due to Persistence and Thickening of the Posterior Fibrovascular Sheath of the Lens, Tr. Ophth. Soc. U. Kingdom **43**:263-272, 1923. Parsons, J. H.: Microscopical Section of Pseudoglioma Due to Congenital Membrane Behind the Lens, ibid. **22**:253-254, 1902. Brückner, A.: Ueber Persistenz von Resten der Tunica vasculosa lentis, Arch. f. Augenh. **56**:5-149, 1907. Lane, F.: Persistent Posterior Fibrovascular Sheath of the Lens, Arch. Ophth. **48**:572-580 (Nov.) 1919. Lent, E. J., and Lyon, M. B.: Persistence of Embryonic Fibrovascular Sheath of the Crystalline Lens, Am. J. Ophth. **5**:706-711 (Sept.) 1922. Gifford, S. R., and Latta, J. S.: Pseudoglioma and Remains of the Tunica Vasculosa Lentis, ibid. **6**:565-571 (July 23) 1923. Fuchs, E.: Pseudophakia Fibrosa of Czermak, in Text-Book of Ophthalmology, ed. 7, Philadelphia, J. B. Lippincott Company, 1923, p. 650.

described in the past [14] as metastatic retinitis, intrauterine endophthalmitis and iridocylitis, congenital falciform retinal fold, opaque membrane behind the lens (Collins and Mayou, 1925), shrunken fibrous tissue cataract (Collins and Mayou, 1925), congenital connective tissue formation in the vitreous chamber (Collins and Mayou, 1925) and fibrous tissue cataract (Mann, 1937).

Both hyperplasia of the vitreous and fibroplasia have in common the persistence of the primary vitreous as the basic congenital lesion. An important difference, however, exists between the two. In the case of persistence and hyperplasia of the vitreous the primary vitreous remains *in toto* and the secondary vitreous forms, so that the primary vitreous occupies its normal position in a funnel-shaped fashion back of the lens. In other words, there has been merely a persistence of the primary vitreous with hyperplasia. In the case of retrolental fibroplasia only a portion of the primary vitreous remains in the region of its base. The important feature seems to be that this persistent primary vitreous is adherent to a portion of the inner layer of the optic cup. As the secondary vitreous forms, it tends to compress and isolate the primary vitreous. This occurs everywhere but in the region where the adhesions have taken place, and here the retina becomes detached. In addition, there may be hemorrhage from the persistent vascular primary vitreous, leading to organization, contraction and further retinal detachment.

Ida Mann [15] in discussing the nature of so-called congenital falciform retinal folds, postulated such an adhesion between the primary vitreous and the inner layer of the optic cup and stated that it must occur at about the 13 mm. stage, which would be about the fifth to the sixth week of embryonic life.

It is conceivable that such an adhesion could be produced by an intrauterine inflammation of the embryonic eye, and in this regard it is known that just at this embryonic period maternal infection can give rise to changes in the eyes of the offspring.

TREATMENT

Eyes with hyperplastic vitreous certainly have the potentiality of vision. The retina in these eyes is in situ and seems to contain all of its cellular elements; the fovea is well formed. Could the pupil be

14. Collins, E. T., and Mayou, M. S.: Opaque Membrane Behind the Lens, in Pathology and Bacteriology of the Eye, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1925, p. 45; Shrunken Fibrous Tissue Cataract, ibid., p. 47; Posterior Lenticonus, ibid., p. 47; Congenital Connective Tissue Formation in the Vitreous, ibid., p. 64. Mann, I. C.: Fibrous Tissue Cataract, in Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, p. 351.

15. Mann, I.: Congenital Retinal Fold, Brit. J. Ophth. **19**:641-658 (Dec.) 1935.

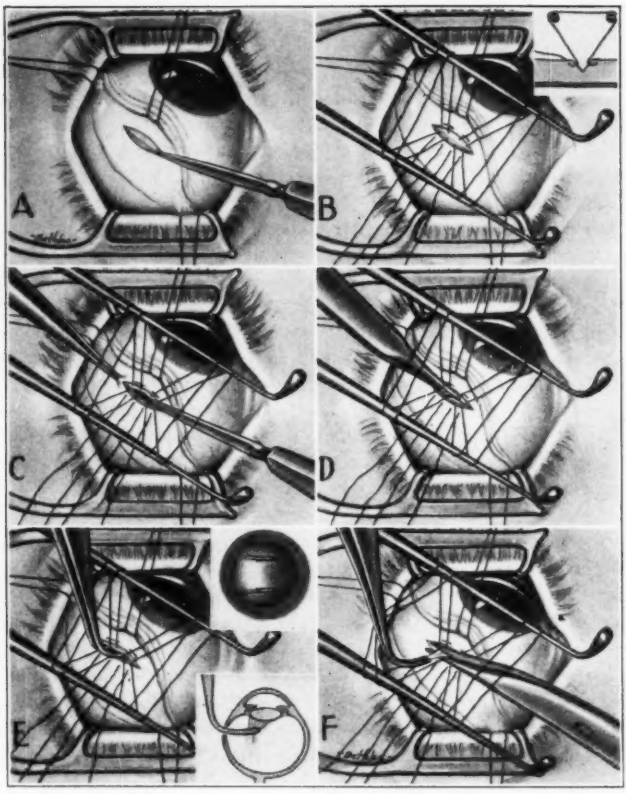

Fig. 15.—Excision of tissue back of the lens.

(*A*) An incision in the conjunctiva over the upper outer quadrant with silk traction sutures under the superior and lateral rectus muscles, as well as through the superficial lamellas of the sclera between 1 and 2 o'clock, 2 mm. from the limbus. An incision 4 mm. long is being made with the scalpel in the sclera for about one third of its thickness concentric with, and 4 mm. from, the limbus. An external canthotomy is usually necessary for adequate exposure. The incision in the sclera should be over the pars planum of the ciliary body and therefore anterior to the ora serrata.

(*B*) Two double-armed, 00000 plain surgical gut sutures are placed through the lips of the incomplete scleral incision. Two strabismus hooks serve not only for retraction of, but also for traction on, the sutures, so that at the site of the incision there is actual negative pressure. The insert shows the depth in the sclera to which the incision is made and the manner of placing the sutures.

(*C*) With negative pressure at the site of the wound, the incision is carried through the sclera at one site.

(*D*) With Stevens' scissors, the incision is enlarged 4 to 6 mm.

(*E*) With Terson's forceps, the wound is entered and the blades of the forceps are directed just posterior to the lens. By looking through the pupil, the blades can be seen magnified (see insert) and the tissue grasped under direct view.

(*F*) An attempt is made to tease the tissue loose and deliver it into the wound for excision. If the tissue is too fixed to deliver, one may free it nasally and pull it temporally sufficiently to free the nasal portion of the pupillary area without excising any of the tissue.

freed of the opaque tissue, there seems to be no reason that the eye would not have vision. In the cases of fibroplasia at least some degree of detachment of the retina is usually present. It is not certain, however, that the retina is always detached and, if detached in only one quadrant, whether or not it remains stationary or progresses. A patient, now 8 years old, with retrolental fibroplasia had the right eye enucleated because it was painful because of secondary glaucoma. The microscopic examination showed retrolental fibroplasia. In the left eye he has retrolental fibroplasia of the type shown in figure 12 and figure 13 *A*. There is a detachment of the retina in the quadrant of the eye occupied by the retrolental tissue. The retina elsewhere is still in situ, after eight years. Except for special schooling, the patient leads a normal life. This 1 case, therefore, indicates that a partial retinal detachment of this nature may remain stationary. In many of the cases it is impossible to say whether or not a detachment of the retina is present and, if so, to what degree. It is probable that in some cases of fibroplasia it is possible to salvage some degree of vision, but certainly in the majority of instances the vision is irretrievably lost because of complete retinal detachment.

In an effort to clear the pupillary area of the opaque tissue in certain indicated cases, I have done in the way of experimental surgery the operation shown in figure 15. This operation has been carried out only on selected eyes, i. e., eyes of about normal size for the age of the patient, eyes in which there is no visible evidence of retinal detachment, eyes in which there are no iris or corneal changes and in which no glaucoma is present.

The operation has been performed on 11 eyes, and in 3 cases there has been objective improvement in that the pupil has been sufficiently cleared to permit a view of the details of the fundus (fig. 16). An opinion, however, regarding the visual results must be reserved because of the age of the patients, the wishful thinking of the parents and the small number of eyes operated on. It can be said, however, that the operation is well tolerated and that no eye has been made worse. Further experience will be necessary in order properly to evaluate the procedure.

In cases of fibroplasia the retrolental tissue may be almost entirely on the temporal side with a much thinner portion nasally. In 1 case the thick tissue on the temporal side could be grasped with forceps and teased away; and, although it could not be drawn out through the scleral opening, it was dislocated nasally sufficiently to free the pupillary area over the nasal portion.

In the way of a surgical procedure, I first attempted repeated needlings, with the idea of getting rid of the lens substance and finally doing a de Wecker discission through the remaining retrolental tissue.

I carried out this procedure on 5 eyes in 5 patients. In the first place, the lens in these eyes did not act like a lens in a normal eye. After an extensive needling procedure, very little happened to the lens. It remained more or less transparent, did not swell and usually only a faint linear scar could be seen in the capsule. In short, this procedure was not at all satisfactory, and it was obvious that nothing could be accomplished by it.

The next procedure I tried was a vertical, through and through discission with a very sharp knife. The section went through the entire lens and the tissue back of it. I did this on 2 eyes in 2 patients. The complete through and through vertical discission was accomplished

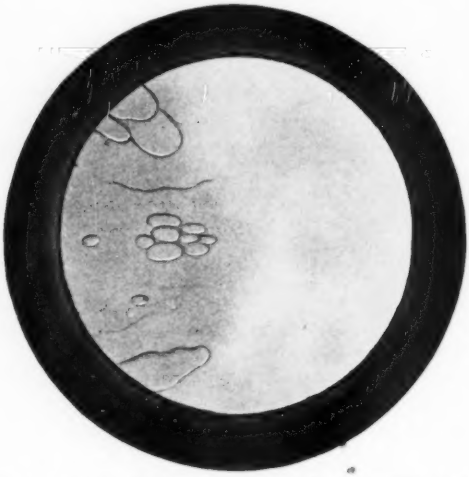

Fig. 16.—Appearance after excision of a sufficient amount of the temporal portion of the tissue to permit a view of the fundus in which no detachment of the retina was seen. There are vacuoles in the posterior cortex of the lens.

without any undue tug or difficulty. The results, however, were complete failures.

Glaucoma is a complication of both hyperplastic vitreous and fibroplasia and the possibility of its occurrence, therefore, is an issue that must be faced. As previously stated, it is not always easy to establish definitely the presence of glaucoma in these eyes because the tonometric readings are probably not always accurate. When glaucoma has been definitely established in eyes in which there may be some potential vision, I have usually tried to combat the glaucoma. Certainly, miotics are of no avail. The operation that I have found most satisfactory is the iridencleisis with sclerectomy.

Sometimes the glaucoma advances sufficiently to create a painful, and obviously useless, eye, which is frequently buphthalmic; then, of course, enucleation is necessary.

We have tried roentgen therapy in 3 cases, employing the same technic as that which is used for retinoblastoma. The technic for retinoblastoma is designed for the maximum effect in the posterior half of the globe. The roentgen ray treatments have not helped in any way, but we feel that we have not given this treatment sufficient trial, and it is our plan to try in at least a few cases a modified technic designed to have the maximum effect in the region back of the lens.

Our hope seems brighter along the lines of prevention, and perhaps through roentgen therapy in the very early stages, before irrevocable damage has been done by progression of the lesion. It is possible that in affected infants the lesion could be detected in its very early stages by adequate examination. If the matrix of the lesion is noted, it may respond satisfactorily to roentgen therapy, as angiomatous tissue, particularly in infants, is known to be radiosensitive.

Dr. Frederick Blodi and Miss Lilly Kneiske gave help in this study.

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ABSTRACT OF DISCUSSION

Dr. Brittain F. Payne, New York: The author has made a differentiation between "retrolental fibroplasia," a name given to postlenticular fibrosis in infants under 3 pounds (1,360 Gm.) by the late Dr. T. L. Terry, of Boston, and "persistence and hyperplasia of the primary vitreous," a term devised by Dr. A. B. Reese and Dr. Frank Payne, of New York, for a similar condition. Although in the earlier stages of the disease the diagnostic points seem clear and definite, as the condition progresses the signs begin to merge, and it is most difficult to determine which condition exists. Sections of the affected eye may give a final clue, but an enucleation is not performed until secondary changes, such as glaucoma and retinal detachment, have occurred. Obviously, the microscopic picture is distorted by these secondary changes, and a true diagnosis is difficult. Little suggestion has been made as to the cause and prevention of these retrolental "changes" in this presentation. The actual mechanics involved in the formation of retrolental fibrosis are somewhat vague and have not as yet been described conclusively. It is possible that "primary vitreous," as generally accepted by most authorities, is actually "secondary vitreous" and forms after the indentation of the ocular cleft and the ingrowth of the hyaloid artery. The primary vitreous would be purely ectodermal and would consist of fibrils extending from the thickening lens placode to the beginning formation of the optic cup up to the 10 mm. stage. The tertiary vitreous would be entirely ectodermal, originating from the ciliary epithelium anterior to the ora serrata. If this reasoning is correct, it is possible that we are discussing persistence and hyperplasia of the secondary vitreous. Just

why the fibrotic changes occur as the embryo develops and become exaggerated after birth is not known. Among the causes given are avitaminosis and intercurrent infections in the mother, but it is also thought that defective germ plasm plays an important role.

The problem of retrolental fibrosis has at least three aspects: 1. Prevention by selection of parents without ocular defects of this type. Let "fate" settle the problem of existence of these defective persons. Obstetricians and pediatricians should not be so zealous in preserving defective persons, of which this world has a sufficient quantity already. 2. Medical and surgical treatment. Therapy has not been successful, but there is hope that more progress will be made as time goes on. 3. The adjustment of the defective child and its family to the unpleasant situation of blindness and dementia. This may be the most important phase.

It is a great privilege to have been asked to discuss this excellent paper on a disease of the eye so little understood and about which so little can be done. The essayist has given us new insight.

Dr. Bertha A. Klien, Chicago: To me the most important statement in Dr. Reese's paper, and one which deserves more emphasis, concerns the frequent association of retrolental fibroplasia with multiple hemangiomas distributed over the body and the presence of angioblastic tissue behind the lens. Angioblastic overgrowth of the primary vitreous in response to some stimulus as yet unknown could occur at any time during gestation after the primary vitreous has started to form. Depending on this time element, the retina is involved in various ways, and different pictures of retrolental fibroplasia may be produced.

On the basis of the histologic material at my disposal, I believe that the matrix of the lesion is present at birth. Occurring early in embryonic life, hemangiomas like these may prevent, partially or completely, formation of the secondary vitreous. Angiomas forming later in remnants of the primary vitreous need not impede normal development of the eye, but may remain latent until some time after birth, when hemorrhages and the sequence of pathologic events, which Dr. Reese described so well, produce the final picture of retrolental fibroplasia.

A recent clinical observation may be of interest. The left eye of a 6½ month old infant, born two and a half months prematurely and weighing 2½ pounds (1,134 Gm.) at birth, was examined. When the infant was 3½ months old, a red area was noted in the left pupil. Six weeks ago, when I saw this patient in consultation with Dr. Kenneth Roper, there was behind the posterior pole of the lens a sharply defined, red area which had a knobby surface and was connected with a large blood vessel; this appeared to be a hemangioma rather than a hemorrhage. If further studies on retrolental fibroplasia should prove beyond doubt the primary role of hemangioma in its pathogenesis, regardless of the cause, as is strongly suggested by the observations of Dr. Reese, then Dr. Reese's modified roentgen therapy might be employed in a preventive manner to the eyes of extremely premature infants of mothers who have a history of systemic disturbances during pregnancy.

DR. HAROLD FALLS, Ann Arbor, Mich.: I should like to take this opportunity to present to the audience preliminary work undertaken to establish the causation of the syndrome under discussion.

My colleagues and I have taken careful pedigrees of all children presenting retrolental fibroplasia whom we have seen. To date we have not discovered any evidence of a hereditary factor. No consanguinity has been found in the fifteen consecutive families studied. In conjunction with the taking of pedigrees, careful serologic studies of the families were made. We were primarily interested in the serologic observations because we desired to establish the correct relationship of the child to the family being studied. Secondarily, we also desired to determine whether the Rh factor or serologic incompatibility played any significant etiologic role. Our excellent and meticulous serologist reported that no serologic incompatibilities had been encountered in a series of 15 children.

Since learning of the work of Drs. Owens and Owens on retrolental fibroplasia, we have had the opportunity of studying 1 child carefully from birth. This was a boy of Mexican ancestry, who was estimated to have been born after six and one-half months' gestation and to have weighed 2½ pounds (1,134 Gm.) at birth. The funduscopic examination, performed three and a half days after birth, revealed what I first thought could only be angiomatosis retinae. The superior and inferior temporal vessels (artery and vein) were huge and tortuous. Moreover, much anomalous branching of these vessels was seen in and about the extreme temporal periphery of the retina. The latter branching occurred in and on a grayish opaque membranous background. When observed over the passing months (nine), the apparently normal retina about and between the temporal vessels became gradually elevated, and slowly tension striae evolved. The vessels slowly diminished in size as they became incorporated in this new gray fibroplastic tissue. Moreover, after observable hemorrhage, the peripheral retina presented fibroplasia, which extended forward and centrally to approach and reach the temporal posterior surface of the lens bilaterally. At no time was there evidence of persistent hyaloid vasculature.

DR. WILLIAM C. OWENS, Baltimore: Three years ago, my coworkers and I decided that if we hoped to observe the clinical course of retrolental fibroplasia, we must observe premature infants from birth. During the past three years, we have been following up, in the Johns Hopkins Hospital, all the premature infants weighing less than 2,000 Gm. at birth. During this time we have observed the development of retrolental fibroplasia in many cases. In none was the disease present at birth. In all cases, the early course of the disease was characterized by dilatation of the retinal vessels with the formation of extensive edematous detachments of the retina. We were able to follow the complete regression of the tunica vasculosa lentis and the hyaloid artery. These structures had completely atrophied before the characteristic changes in the retinal vessels began. We have never seen retrolental fibroplasia develop from, or in, a persistent hyaloid artery or primary vitreous. The final picture has varied considerably, depending on the severity of the disease. We have observed during

their development the various examples of the disease shown by Dr. Reese and the discussers. During the inactive, late, stage of the disease, it is usual for the vessels in the membrane to decrease in size. We have also seen several cases in which the disease regressed spontaneously.

DR. ALGERNON REESE, New York: Dr. Payne stated that no mention has been made of the etiologic factors. Needless to say, the cause of retrolental fibroplasia is not known, but in the paper I included various possible causative factors, such as maternal infection, lack of vitamin A and anemia. Dr. Klien has shown us some excellent sections illustrating the pathologic changes. Her specimens seem to bear out the contention that the basic lesion in retrolental fibroplasia is persistence of the vascularized primary vitreous in the region of its base. I am grateful to Dr. Owens and Dr. Falls for their comments.

HISTOPATHOLOGIC ASPECTS OF RETROLENTAL FIBROPLASIA

BERTHA A. KLIEN, M.D.
CHICAGO

MUCH has been accomplished by various authors (Reese,[1] Krause,[2] Ingalls,[3] Owens[4]) in clarifying the confusion of multiple terms and descriptions of apparently related conditions since Terry[5] first drew attention to a disturbance connected with prematurity to which he applied the not very appropriate, but in ophthalmologic circles now almost generally accepted, term of retrolental fibroplasia.

The pathogenesis of retrolental fibroplasia and of the conditions apt to be confused with it is of two principal, and essentially unrelated, varieties.

The first type, apparently not connected with maternal-fetal infection or premature birth, is characterized by arrest of embryonic growth, with or without aberrant growth of the involved tissues. There is commonly a familial or hereditary background, and more often than not the condition is unilateral. These genetically predetermined maldevelopments may have their inception at any period of gestation and range from complete failure of primary retinal coaptation in more or less microphthalmic eyes to mere persistence of the hyaloid artery.

Retrolental fibroplasia is represented by the second group of cases. The bilateral occurrence, the extremely premature birth and the frequency of uterine bleeding during gestation cited by various authors suggest immediately a more direct and severer disturbance in the maternal-fetal relationship. This type of lesion is often not discernible at birth but becomes evident two to five months later.

On the basis of the histologic material at my disposal, I agree with Reese[1] that the matrix of the lesion is present at birth. The

From the Department of Ophthalmology, Northwestern University Medical School.

1. Reese, A. B.: Persistence and Hyperplasia of Primary Vitreous (Tunica Vasculosa Lentis or Retrolental Fibroplasia), Am. J. Ophth. **29**:1, 1946.

2. Krause, A. C.: Congenital Encephalo-Ophthalmic Dysplasia, Arch. Ophth. **36**:387 (Oct.) 1946.

3. Ingalls, T. H.: Congenital Encephalo-Ophthalmic Dysplasia, Pediatrics **1**:315, 1948.

4. Owens, W. C., and Owens, E. U.: Retrolental Fibroplasia, Baltimore, Wilmer Residents Association, 1948.

5. Terry, T. L.: Fibroplastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants, Am. J. Ophth. **25**:203, 1942.

most important statement concerning the pathogenesis of retrolental fibroplasia, and one which deserves more emphasis, has been made in one of Reese's [6] recent papers. It concerns the frequent association of retrolental fibroplasia with multiple angiomas distributed over the body and the presence of angioblastic tissue behind the equatorial region of the lens, demonstrated histologically.

HISTOPATHOLOGIC REPORT

The histopathologic changes in 3 eyes with retrolental fibroplasia are discussed.

CASE 1.—R. E., a premature infant, was first seen at the age of 3½ months.

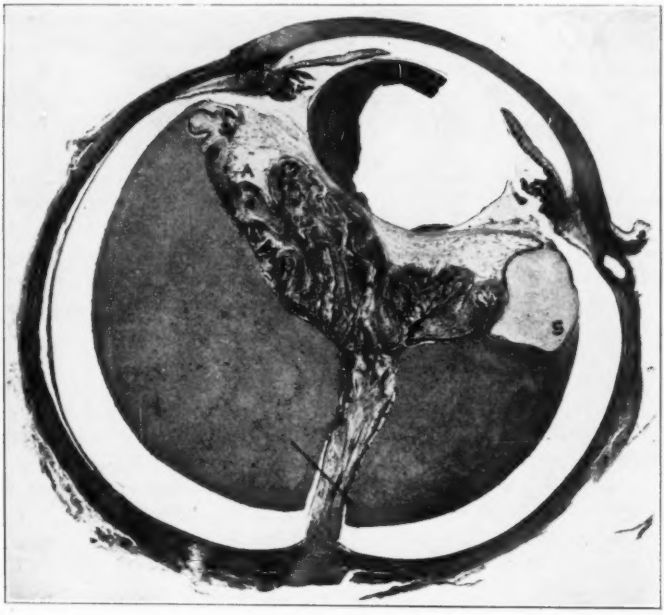

Fig. 1 (case 1).—Right eye. *S* indicates a rudimentary secondary vitreous; *A*, angiomas invading the retina.

Information regarding the maternal history, weight at birth and degree of prematurity could not be obtained. Ten days prior to the first examination the mother had noted a gray reflex from the right pupil.

Clinical Findings.—Right Eye: The anterior chamber was extremely shallow. In the nasal half of the globe there was a grayish mass with superficial blood vessels behind the lens. A red reflex was obtained from the temporal side.

6. Reese, A. B.: Persistence and Hyperplasia of Primary Vitreous; Retrolental Fibroplasia: Two Entities, Arch. Ophth., this issue, p. 527.

Left Eye: Through the dilated pupil a gray mass was visualized in the region of the nasal portion of the ora serrata. Above and below this mass and in the temporal part of the retina were large whitish areas. The optic disk was not visible, and there were only a few visible retinal vessels. These were seen best with a —14.00 D. lens.

General Physical Condition: The general condition was normal except for a small umbilical hernia.

Course.—The diagnosis of bilateral retinoblastoma was made, and the right eye was removed. Radiation therapy of the left eye was carried out for the following five months. At the end of this period the left eye was removed also.

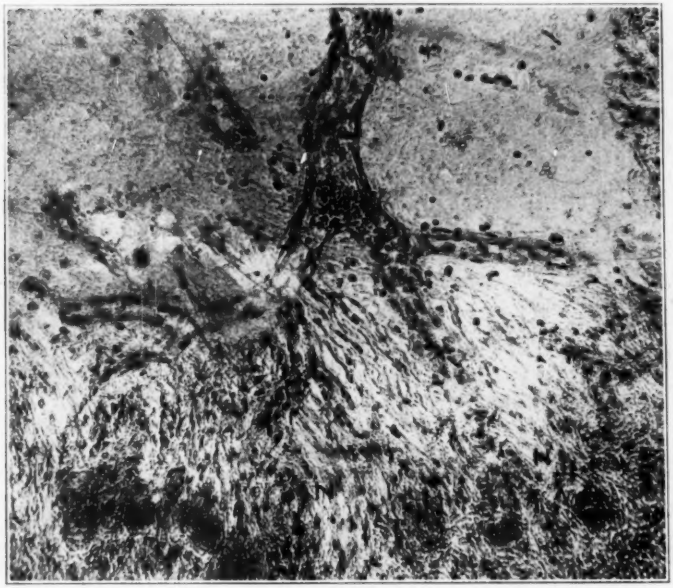

Fig. 2 (case 1).—Right eye: magnification of area *A* from figure 1, showing blood vessel in remnants of primary vitreous sending finger-like extensions into retina. *N* indicates nodules of proliferated endothelial cells.

Histologic Study.—Right Eye: The bulb measured 17 mm. in the sagittal, 18 mm. in the frontal and 19 mm. in the vertical diameter. The horizontal diameter of the cornea was 10 mm. The anterior chamber was shallow; the structures of the angle of the chamber were well developed, but a fan-shaped, delicate mesodermal tissue lay between the trabeculum and the anterior chamber. The iris was very cellular, with an undeveloped pattern of the anterior surface. The lens measured 4 by 5.5 mm.; the zonular fibers were well developed. The retina contained rosettes and pseudorosettes and was folded into a funnel-like mass, lying in the axial direction (fig. 1). Between the retina and the equatorial region of the

lens were extensive remnants of the primary vitreous, which contained a large number of angiomatous, thin-walled blood vessels. Some of these vessels sent finger-like extensions into the adjacent retina, and at the end of each intraretinal sprout were nodules, consisting of proliferated endothelial cells (figs. 2 and 3). The remnants of primary vitreous contained small, free hemorrhages here and there and at the border of the adjoining rudimentary secondary vitreous there was a wall of fibrous tissue, which represented organization products of hemorrhages. The subretinal space was filled with a homogeneous coagulum. Pigment epithelium and choroid appeared normal.

Left Eye: The bulb measured 19 by 17 by 20 mm. The cornea had a horizontal diameter of 10 mm. The structures of the angle of the chamber were well devel-

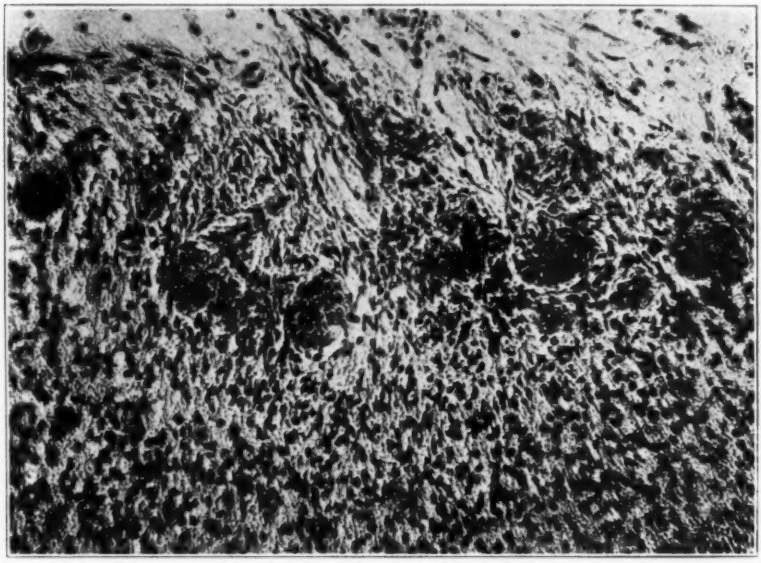

Fig. 3 (case 1).—Right eye: nodules (*N*) of proliferated endothelial cells in focus.

oped, but the angles were obliterated by extensive anterior synechias. The iris was atrophic and covered with a thin fibrous membrane, which had caused a marked ectropiom of the pigment epithelium on one side and almost a reduplication of the iris on itself on the other side. The lens measured 4.5 by 6 mm.; the zonular fibers were well developed. The superior and temporal portions of the retina were artificially detached and showed marked dysplasia, consisting of a thin, almost completely glial membrane. The inferior and nasal portions of the retina were folded into a falciform structure (fig. 4), outside of which there was graunlar coagulum. The optic nerve head was drawn toward this retinal fold and there was considerable supertraction of the opposite part of the retina, or

possibly a persistent dorsal retinal fold. Between the falciform retinal fold and the equatorial region of the lens was a network of thin-walled, tortuous vessels within a delicate scaffolding of connective tissue. Some of these vessels entered the retina (fig. 5), coursing within it for some distance and then returning to the remnants of primary vitreous. The pigment epithelium was normal, except just above the nerve head, where it had proliferated as though stimulated by traction.

In both eyes of this patient there was extensive failure of primary retinal coaptation and of formation of secondary vitreous, and not a true retinal detachment.

CASE 2.—This case illustrates a type of retrolental fibroplasia different from that just described, and apparently the one more frequently encountered. A. L.,

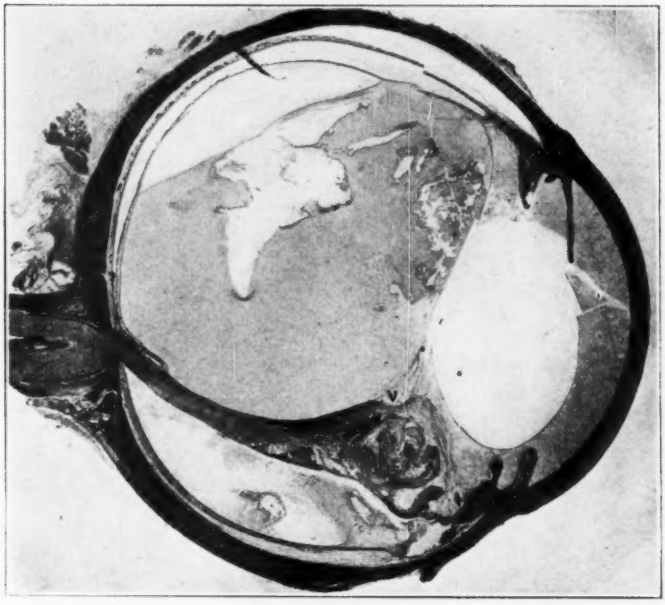

Fig. 4 (case 1).—Left eye, showing falciform retinal fold. *V* indicates vessels in remnant of primary vitreous.

aged 10 months, born six and one-half months prematurely, weighed 22 ounces (624 Gm.) at birth. At the age of 3½ months a white reflex from both pupils was noted by the mother. During the past few weeks the child seemed to have had discomfort in his left eye.

Clinical Findings.—Right Eye: The anterior chamber was extremely shallow. Behind the lens, the anteroposterior diameter of which appeared somewhat diminished, there was a grayish white tissue with blood vessels visible on its surface.

Left Eye: The ciliary body was mildly injected. The anterior chamber was extremely shallow, and just nasal to the center the iris was in contact with the

cornea, the surface of which was slightly stippled. Otherwise the picture was similar to that of the right eye. The tactile tension of the left eye seemed increased.

General Data: The general physical findings were normal. The weight at the age of 10 months was 11 pounds 7 ounces (5,188 Gm.).

Course.—The left eye was removed, because the secondary glaucoma raised the suspicion of a retinoblastoma.

Histologic Study.—Left Eye: The sagittal diameter was 17 mm., the frontal 17 mm. and the vertical 18 mm. The cornea measured 8.5 by 9.5 mm. There were

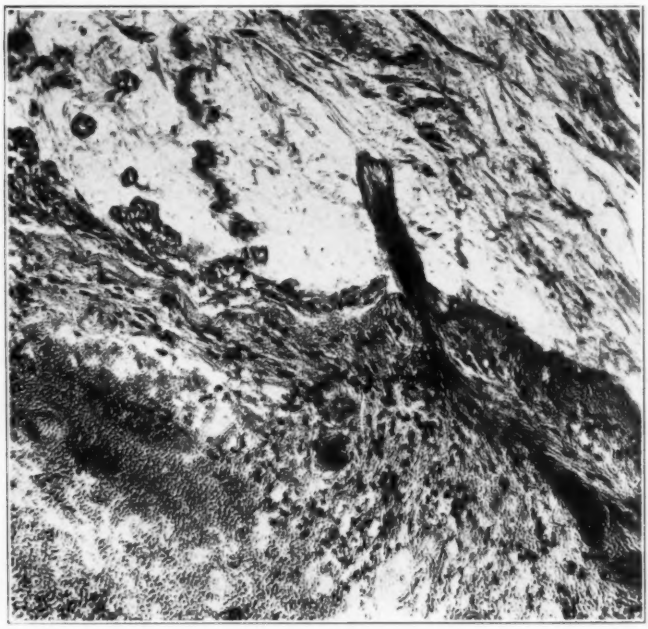

Fig. 5 (case 1).—Left eye: magnification of area at *1'* in figure 4, showing blood vessel entering retina from primary vitreous.

short peripheral anterior synechias and below the center of the cornea a more extensive anterior synechia, which had led already to formation of a substance between the cornea and the iris resembling Descemet's membrane. The pupillary borders were adherent to the lens, which had an anteroposterior diameter of 2.5 mm. The iris was greatly atrophied. The ciliary body was drawn inward; some of its processes were elongated, and the pigmented and nonpigmented epithelium showed excessive proliferation. There was an axial detachment of the retina (fig. 6). The retina was degenerated and formed many pseudorosettes. It was suffused with blood, especially behind the temporal equatorial region of the

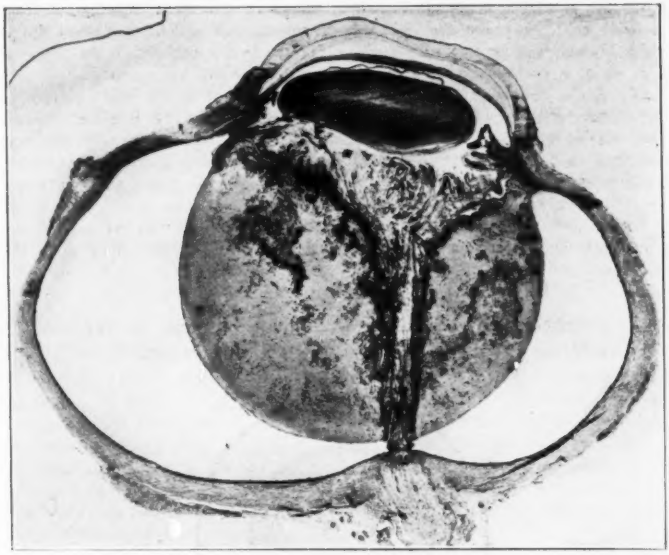

Fig. 6 (case 2).—Fibrous tissue (*F*) between retina and equator of lens, containing many tortuous, partly collapsed blood vessels.

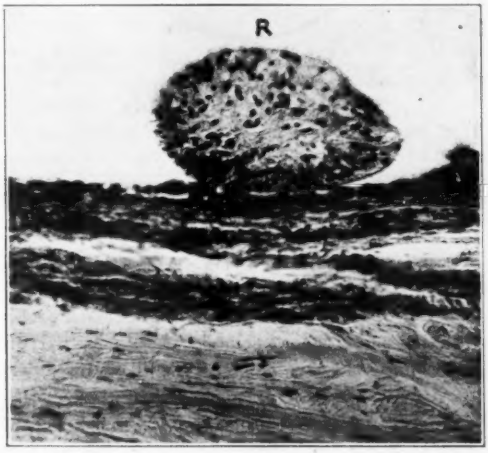

Fig. 7 (case 2).—Torn out piece of retina (*R*) adherent to pigment epithelium.

lens. The subretinal coagulum contained masses of cholesterol crystals and fatty granular cells. Between the lens and the retina was a delicate fibrous tissue, which became broader toward the equator of the lens, especially on the temporal side, where it contained a network of thin-walled, partly patent, partly collapsed blood vessels. Some of these vessels were creeping along the inner surface of the retina. Plaques of denser fibrous tissue, surrounded by free hemorrhage, were applied to the surface of the retina in several places. The choroid was shrunken as a result of fixation but appeared normal. There was irregular proliferation of the pigmented epithelium, and in several places torn-out pieces of retina were adherent to its inner surface (fig. 7).

In this case the shreds of retina still adherent to the choroid indicated a true retinal detachment, and not a failure of primary retinal coaptation, as in the first case.

COMMENT

Angioblastic overgrowth of the primary vitreous in response to some disturbance as yet unknown—anoxia was suggested by Ingalls

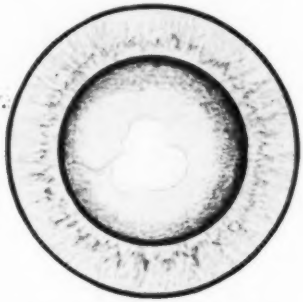

Fig. 8 (case 3).—Large blood vessel behind lens connected with knobby, reddish area with appearance of a hemangioma.

—may occur at any stage of gestation after formation of the primary vitreous has started. Depending on this time element, the retina may be involved in various ways, and different histologic pictures of retrolental fibroplasia may be produced.

Occurring in the primary vitreous early, before the 13 mm. stage, as in the eyes in the first case discussed here, these angiomas, by invading the retina, may more or less extensively prevent primary coaptation of the retina and formation of the secondary vitreous. No inflammatory lesion need to be assumed to explain the firm attachment between primary vitreous and retina in these cases.

Angiomas forming within remnants of the primary vitreous at a later stage need not interfere with normal development of the eye and might remain latent until some time after the premature birth, when hemorrhages and their organization products behind the equa-

torial region of the lens and near the base of the vitreous begin to exert traction on the retina and lead to its detachment.

A good example of a disease which is based on a congenital anomaly but may remain latent for two or three decades is von Hippel–Lindau angiomatosis. The angioblastomas in the retina and the central nervous system which characterize this disease have their inception, according to Lindau, during the third month of fetal life but do not become manifest until late in adult life.

Once the full picture of retrolental fibroplasia has developed, hemangiomas may become lost within the shrinking fibrous tissue and the masses of proliferated pigmented and nonpigmented epithelial cells of the ciliary body, and in histologic preparations of old cases of retrolental fibroplasia they may be difficult to demonstrate.

In this connection, a recent clinical observation may be of interest.

CASE 3.[7]—M. R., a 6½ month old infant, born six and one-half months prematurely, had a weight at birth of 2½ pounds (1,134 Gm.). Bilateral retrolental fibroplasia was first noted at the age of 3 months. At the same time a reddish area was observed in the left pupil. At the time of the first examination, at the age of 6½ months, there was behind the posterior pole of the lens a well defined, red area with a knobby surface, which was connected with a large blood vessel and had the appearance of a hemangioma, rather than of a hemorrhage present for three months (fig. 8).

If further studies should prove beyond doubt the primary role of hemangiomas, regardless of their cause, in the pathogenesis of retrolental fibroplasia, an origin which is strongly suggested by the histologic material presented by Reese and myself and by some clinical observations (Reese,[6] Ingalls[8]), then Reese's modified roentgen therapy could be employed in a preventive manner to the eyes of extremely premature infants of mothers who give histories of uterine bleeding or of other systemic disturbances during gestation.

109 North Wabash Avenue (2).

7. This patient was seen in consultation with Dr. Kenneth Roper.

8. Ingalls, T. H.: Epidemiology of Encephalo-Ophthalmic Dysplasia, J. A. M. A. **138**:261 (Sept. 25) 1948.

DIVERGENCE INSUFFICIENCY AS A PRACTICAL PROBLEM

L. WESTON OAKS, M.D.
PROVO, UTAH

DIVERGENCE insufficiency is a definite clinical entity. It exists as a practical problem, irrespective of whether pros or cons dominate the perpetual argument over existence of a divergence center in the brain.

The variety of definitions in the literature suggests some confusion as to the characteristics and nature of the condition. Generally, it is the impression that differences of expression arise largely from a paucity of case studies carried out to reasonable completion. Thus, one writer draws conclusions from use of the Maddox rod and taking of ductions with Risley prisms. Another uses only the findings of prism-screen tests. Another allots more importance to lateral vergences at near points and tries to delegate to them arbitrary "normal" values, by which to be guided.

It seems to matter little whether one considers divergence as an active process presided over by a brain center, located near the nuclei of origin of the abducens nerve, or goes along with Scobee,[1] when he says:

> Evidence has been produced (Scobee and Green 1946) which indicates that esophoria and exophoria are not two separate entities but merely varying degrees of the same thing. In the light of this fact, the etiology of esophoria and exophoria should be similar in the sense that etiologic factors playing upon the convergence center might result either in a hypertonic state (esophoria) or a hypotonic state (exophoria).

Two things appear to be important: (1) to recognize that the clinical entity does exist with sufficient frequency to represent an important part of the daily refraction patients, and (2) to see that, if one is to appreciate properly the need for treatment of such a patient, data must be carefully obtained.

Cases of divergence insufficiency are not rare. In an analysis of 2,600 refractions, I found this problem appearing in 129, or nearly 5 per cent. This number included only patients in whose examinations

Read before Pacific Coast Oto-Ophthalmological Society, Seattle, June 9, 1948.

1. Scobee, R. G.: The Oculorotary Muscles, St. Louis, C. V. Mosby Company, 1947, p. 136.

two or more of the tests used indicated divergence insufficiency. Not included were 175 others for whom one measurement indicated the defect—usually the reading in the prism-screen test or values for lateral vergences at near points. These patients, although many of them offered the same complaints (headaches, dizziness, ocular fatigue, blurred vision for distance) as did the others, were excluded on the grounds that the symptoms probably resulted from errors in refraction. Undoubtedly, some of them will show gradual increase in the divergence insufficiency and later will be found to need care for it.

In order to acquire dependable data on the problem, one must be aware of its chief characteristics. Because of the close relation between divergence insufficiency and convergence excess, some confusion has found its way into descriptions of this condition.

Scobee's [2] definition is:

> . . . (3) Divergence insufficiency—if there is either exophoria or exotropia, and it is greater at near than at far, there is divergence insufficiency.

This specification appears unnecessarily involved.

Duane [3] defined the deficiency thus:

> . . . Weakness of the diverging power, characterized by the following signs:
>
> For Distance.—Esophoria of varying amount . . . by all tests (phorometer, screen and parallax). Associated lateral movements normal. Diverging power very much reduced, the reduction being proportionate to the degree of the the esophoria.
>
> Prism convergence (adduction) normal, or often somewhat deficient. Exercise of the convergence often gives rise to a temporary homonymous diplopia, and the latter may also in some cases . . . occur spontaneously, or be evoked by simply placing a red glass before one eye.
>
> For Near.—Signs, unless the condition is associated with a convergence insufficiency or with a convergence excess, fairly normal.

This statement seems sufficiently clear to admit of its being understood as a practical working formula. Briefly, one might start with the premise of an esophoria for distance that is reduced at the near point and which increases in amount as the distance is lengthened.

Both Duane [3] and White [4] expressed the feeling that great care should be taken in diagnosis of these cases of divergence insufficiency, since in each the defect may be combined with, or may grow out of, an actual convergence excess or convergence insufficiency. They cautioned, further, that care be used to determine that the given patient

2. Scobee,[1] p. 250.

3. Duane, A.: (*a*) A New Classification of the Motor Anomalies of the Eye, Ann. Ophth. & Otol. **5**:969-1008, 1896; **6**:84-122 and 247 and 260, 1897; (*b*) New York, J. H. Vail & Co., 1897, pp. 83-84.

4. White, J. W.: Unpublished lectures at New York Post-Graduate Medical School and Hospital, 1943.

is not really the victim of a mild or moderate paresis of one or both lateral rectus muscles.

In acquiring data from patients here studied, the tests used were divided into two groups, determinative and corroborative. The following tests were considered of determinative importance:

1. Screen-prism measurements. (*a*) The muscle light was at the usual distances; then, in cases in which divergence insufficiency was suggested, the measurement for distance was repeated at from 500 to 5,000 feet (150 meters to 1.5 kilometers), or farther. One should not be satisfied in using the prism-screen test for possible divergence insufficiency with measurement for distance taken only at 20 feet (6 meters). More information may be acquired with the patient facing a window—or moved out of doors—where an object at 500 to 5,000 feet may be had for him to fix on.[5] When this type of imbalance is present, the esophoria will be increased at the greater distance and much diminished at the near point of 30 cm. (*b*) The same test is next carried out at 50 cm. with the eyes in the six cardinal positions to determine any individual muscle weakness. (*c*) Screen-prism measurements should always be preceded by observation of ocular movements, in order to discover possible lagging in any position. The combination of these three details gives ready and dependable evidence of individual muscle weakness.

2. Prism duction tests for distant and near vision, with both breaking and refusing points recorded with Risley prisms on the phorometer. These duction measurements usually reveal a divergence insufficiency, especially in the recovery of abduction at the near range. While this test has been demonstrated by experience to be dependable in the majority of cases, it is insufficient as a basis for diagnosis, since it is subject to serious limitations, especially in its subjective nature, and in the suppression so often shown by patients with mild or severe muscular imbalances.

Use of the rotary prisms, with lights for targets, invariably brings into play numerous reflections, prism "moons," all of which distract the attention of the uninitiated. In vergence tests with Risley prisms, suppression often poses some difficulty. Among the 2,600 patients in the total group, 576 suppressed to an extent interfering with satisfactory prism duction tests.

3. Lateral prism vergence at the near point (33 cm.). Results of convergence and divergence tests at the near point furnish valuable data in any case of muscular imbalance with binocular vision. About ten years ago I began regularly taking convergence and divergence

5. White, J. W.: Divergence Insufficiency and Palsy, New York State J. Med. **47**:63-65 (Jan. 1) 1947.

readings at 13 inches (33 cm.). A large number of such observations seem to show that certain textbooks on refraction are in error when they state that the values for convergence at the near point should always be larger than those for divergence at the near point. As a matter of fact, it is easily demonstrated that any patient with such a relation between convergence and divergence has discomfort, growing out of some measure of divergence insufficiency or convergence excess or both. Except in certain cases of myopia, correction of refractive errors alone will not relieve the patient's troublesome symptoms. In the average case of hypermetropia, astigmatism or compound errors, it appears desirable for visual comfort to have the divergence at 33 cm. 25 to 50 per cent greater than the convergence at that distance, although a patient may have visual comfort so long as divergence is not less than the convergence.

Lateral prism vergence at near point is measured with the patient wearing the correction for distance—not with a light for fixation, as in the measurement of ductions, but with a black dot or vertical line on a white card. The patient is instructed to hold the spot or line against breaking, while prism, base out or base in, is gradually increased to bring diplopia.

Scobee [6] stated:

> . . . I prefer to use an arbitrary limit of fifteen prism diopters of divergence at the reading distance as "normal." If the patient's prism divergence is not at least fifteen prism diopters, one can be reasonably certain that glasses alone will not relieve the patient's symptoms.

It is common experience in all muscle work that little dependence can be placed in any arbitrary standard one sets up, even as a guide, unless one is fully aware of the weaknesses in its use. There are patients who have a sthenic type of response of the extraocular muscles whose convergence at the reading distance may measure 25 to 30 △. By the same token, their normal prism divergence should be more than that amount, or at least its equivalent. Again, one sees persons whose responses are quite the opposite—whose convergence at 13 inches is 9 to 10 △. For such a return on the convergence, a value of 15 △ of prism divergence at the near point would suffice. Both types may have normal balance of the extraocular muscles.

Among tests that are made to establish the diagnosis, but which actually offer only corroborative information, the following were used in all cases: 1. Maddox rod and prism on the phorometer. This test, to determine the amount of esophoria, was perhaps used rather as a matter of habit and could readily have been discarded with little effect on the results. 2. Near point of convergence (PcB) at the base of the eyes. This should normally be 95 mm. or less.[3] Among patients with

6. Scobee,[1] p. 261.

divergence insufficiency here covered, the measurements for near point of convergence averaged about the same as they did for the whole group. This is in accord with Duane's statement [3] that the near point of convergence is normal. 3. Interpupillary distance. One might expect this measurement to be short in such cases if there were a close association, in anatomic setup, between divergence insufficiency and convergence excess. Among these patients, 29 had an interpupillary distance of less than 60 mm. The majority of them had between 60 and 65 mm., and 22 showed measurements between 65 and 75 mm.

In diagnosis of muscle problems, it is vital to keep in mind the following points: (*a*) Theoretic and mathematically calculated arbitrary values will lead one into error, both in estimating a patient's needs and in one's performance of surgical corrections on such a basis, and (*b*) any formula one sets up by which to evaluate abnormalities must be broad and flexible, so that there is no temptation to crowd an individual case into an established pattern. No system of values one might arrive at will ever be an acceptable substitute for careful study of each patient's problem on its own merits. There is probably no part of medical practice in which this is more true than in the study and treatment of heterophorias and squints.

The cause of divergence insufficiency has been most commonly identified with progressive convergence excess.[7] Duane [7b] and Fuchs [7c] each considered it both primary and secondary, usually the latter. Fuchs stated that about the only example of primary divergence insufficiency was the divergence palsy of supranuclear origin.

Duane [7b] stated:

> Uncomplicated idiopathic divergence-insufficiency is comparatively rare, and, moreover, some of the cases that would seem to fall into this category are probably either really secondary to some disorder of the vertical muscles (elevators or depressors), or are examples of a spurious divergence insufficiency, i. e., of a condition in which there is actual weakness of the externi themselves, either natural or produced by operation. In cases of the latter kind the divergence is indeed weak, but the power of making lateral movements is also lessened, and hence these cases do not come fairly under the head of a simple impairment of diverging function.
>
> Complicated idiopathic divergence-insufficiency is more common. In these cases there is either a convergence-insufficiency which has developed simultaneously with the disorder of divergence, or there is a convergence-excess which is the result of the latter.

Of the 129 cases in the present series, signs of convergence excess were present in only 21. As to the frequent association of divergence

7. (*a*) Scobee.[6] (*b*) Duane.[3] (*c*) Fuchs, E.: Fuchs's Text-Book of Ophthalmology, authorized translation from the twelfth, revised and greatly enlarged German edition, with numerous additions, by A. Duane, ed. 5, Philadelphia, J. B. Lippincott Company, 1917, p. 781.

insufficiency and disturbance of vertically acting muscles,[8] hyperphoria of 1 △ or more occurred in only 19 of the series. The ages in these cases ranged from 6 to 70 years, with no significant age grouping, except that four fifths of the patients were under 40 years of age. This is not greatly at variance with the percentage of ophthalmic examinations done which fall in that age group.

By analogy, it is only reasonable to consider that divergence insufficiency is no more properly a strange interloper than is convergence insufficiency, convergence excess or divergence excess. The same influences that operate for or against the occurrence of one type may be just as potentially effective in producing another.

Besides the great complexity of the mechanism involved, the very nature of neuromuscular function, especially under stress, favors troublesome combinations. Predication of serious disease of the brain is no more necessary to account for insufficiency of the divergence function or faculty than to account for other insufficiencies or excesses.

In the symptomatology, headache plays a prominent role. In 65 of the 129 cases it was the chief complaint. Next came ocular fatigue, complained of with both near work and distant use of the visual apparatus. Occasional diplopia, nausea, dizziness and blurring of vision—especially for distance, but also for near vision—were encountered. Panoramic headaches, train and car sickness were mentioned by White.[4] Nervous instability was included by Prangen and Koch.[9]

Bruce [8] noted palsy of the lateral rectus muscles late in these cases, indicating that in some the condition is steadily progressive toward that ultimate goal. White [4] stated that some patients require repeated surgical procedures at irregular intervals over the years to maintain visual efficiency. Undoubtedly, these patients represent the severest form, just as one sees patients with convergence insufficiency that is equally difficult to deal with.

Treatment of divergence insufficiency must meet the same general requirements as treatment of other disturbances of vergence integrity—satisfaction of the needs of each individual problem on its merits. The patients should be instructed not to sit far back at the theater, but to locate themselves about fifteen to twenty rows from the front. Beyond some such point, their discomfort will increase with their distance from the screen. For those with presbyopia among them, the reading addition should be attended to, since some patients will be more comfortable in reading at less than 15 inches (33 cm.). In a few cases, with mild hypermetropia, the addition of a $+\frac{1}{4}$ to $+\frac{1}{2}$ D. sphere (depending on the patient's comfort) to the correction for each eye will be accepted and will give relief from milder symptoms.

8. Bruce, G. M.: Ocular Divergence, Arch. Ophth. **13**:639 (April) 1935.

9. Prangen, de H., and Koch, F. L. P.: Divergence Insufficiency, Am. J. Ophth. **21**:510 (May) 1938.

For most patients with myopia of more than 1 D., no treatment, except for proper refraction and correction, will be required, unless the condition is pronounced and accompanied with considerable headache. This fact appears to be related in some way to the lower degree of tonus in convergence function present with myopia.

In the application of glasses to the correction of divergence insufficiency, one must consider also the use of base-out prisms. These have been both praised [8] and condemned.[9] Duane [10] stated:

> The constant wearing of prisms, base out, is in most cases a dangerous expedient, as tending to cause disuse and a consequent further enfeeblement of the abduction power.

It is true that many such patients cannot wear base-out prisms with any degree of ease, but there are others who accept them gratefully and are relieved of discomfort. They wear the same glasses for near work without any apparent disadvantage. I have yet to see the first of the patients show any progression of his imbalance with wearing base-out prisms. Several have improved with such care to the point where the prisms were removed without further symptoms being experienced.

As previously stated, some of these patients, with approximately the same degree of trouble as others who are benefited, cannot wear the prisms or are not made comfortable by their application. So far as I know, there is no way by which one may determine to which group a given patient belongs except by applying base-out prisms in a trial frame and having the patient read with them for a time. One may begin with 1 D. prisms or ½ D. prisms, depending on the findings, and then increase or decrease the strength, as the case may be, until a comfortable level is found or it is discovered that no combination increases the ease of reading. Theoretically, such determination should be made for distant vision, but in actual practice, the prism the patient accepts at the near point gives relief for distance as well.

Important as well in the scheme of therapy is orthoptic training. This, too, has suffered both condemnation and commendation. Again, it is probably a matter of proper determination as to which measure is suitable for which patient. Orthoptic training, properly carried out, can be, and has been, of great help to many of these persons.

Undoubtedly, those persons who are rapidly benefited by base-in training were victims of a state of unsteady coordination of the horizontally acting rectus muscles. Clinically, this reveals itself in frequent spasms of muscles while prism ductions are being taken. Often successive trials of the same test give widely disparate results.

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10. Duane,[3b] pp. 85-86.

Patients with divergence insufficiency which is not of sufficient severity to demand surgical intervention should be given the benefit of orthoptic care for a few weeks. Such patients are much slower in response than are patients with convergence insufficiency. Two treatments in each of six weeks may be necessary before any real benefit is apparent. By the end of such a period it should be possible at least to say whether the training offers a chance of helping the patient. For some the sessions must be continued for about three months to insure comfort and easy use of the eyes. A few patients will experience recurrence and may require a second series of treatments, but most of them appear to establish better visual habits and to be permanently relieved.

Patients who will require surgical treatment, and who have no prospect of help from orthoptic training, may usually be recognized within the first three weeks of their treatment. Operation is perhaps best done first on the nondominant eye. White [4] has called attention to the desirability of not doing too much at one time on such a patient, advising the shortening of one lateral rectus muscle, and then, later, of the other if it becomes necessary.

Certainly, it is unwise, if not disastrous, to attack a medial rectus muscle in a case of this kind when the near point of convergence is not definitely closer than normal. The O'Connor cinch shortening operation serves excellently the needs of such patients. It is simple; it can be repeated if necessary, and it gives immediate results, without prolonged postoperative disability.

SUMMARY

Divergence insufficiency is a definite clinical entity. It occurs, in some degree, in more than 10 per cent of all cases of refraction in which there is binocular vision. The condition is characterized by esophoria which is greater for distance than for near vision. The cause is uncertain, but there seems no reason that the condition should not occur from the same causes that produce other imbalances of the horizontally acting muscles. Symptoms include headache (not relieved by correction of refractive errors), ocular fatigue and occasional diplopia, nausea, dizziness, blurring of distant vision and panoramic headache.

Detection and diagnosis are accomplished by use of screen-prism tests, prism duction measurements and lateral vergences tests at the near point. The relation of convergence and divergence at the near point are found not to conform to statements in some textbooks. Treatment is best accomplished by (1) proper refraction, (2) increase in the plus sphere correction, (3) use of base-out prisms, when accepted, (4) orthoptic training and (5) surgical intervention.

23 East Second South Street.

AN EARLY PHOTOGRAPH OF VON HELMHOLTZ WITH EXPLANATORY LETTER

JOSEPH C. AUB, M.D.
Professor of Research Medicine, Harvard Medical School
BOSTON

The accompanying letter was written by Prof. Ernst von Brücke a few months before his death.[1] He had been professor of physiology at Innsbruck before coming to Boston.

Boston, Dec. 22, 1940

My dear Dr. Aub:

Ninety-four years ago, in 1846, my grandfather studied the reflection of light from the background of the human eye. It was this work that stimulated Brücke's friend, von Helmholtz, to invent the ophthalmoscope. My grandfather was the first one on whom von Helmholtz tried his instrument and the first person in whom he saw the background of the living eye.

These facts came back to me when you inspected my own retina, and I thought you might be interested in an old (so far as I know unpublished) daguerreotype of von Helmholtz (about 1848) which he gave to my grandfather. I should be happy if you would do me the favor of accepting it as a small token of sincere gratitude.

With very best wishes for Xmas and for a happy new year,

As ever yours,

E. Brücke.

The daguerreotype has apparently not previously been published, although it obviously was taken the same day as the one from the collection of Prof. Dr. Claude du Bois-Reymond, dated March 23, 1848, and published in Koenigsberger's life of von Helmholtz [2] in 1903. The picture thus was made one hundred years ago.

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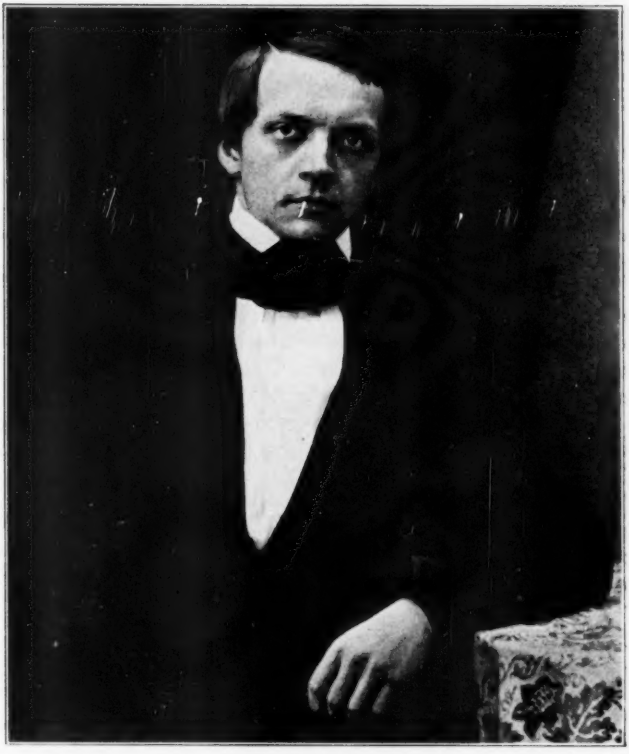
1. It is not generally recognized that Brücke, referred to in the letter, came near to being the discoverer of the ophthalmoscope. As quoted in Sigerist's "The Great Doctors," von Helmholtz stated: "I had to explain to my pupils the theory of the retinal reflex, which originated with Brücke. Brücke only just failed to discover the ophthalmoscope. He failed because he had not asked himself to what optical image the rays reflected from the illuminated eye belong. For his purposes, at the time, this question was superfluous. Had he asked it, he would have found it just as easy as I did to answer it, and the ophthalmoscope would have come into existence earlier than it did . . . . At first I found it difficult to use. Had it not been for my firm theoretical conviction that it would be possible to see the fundus, I might not have persevered. But after about a week I was the first who ever succeeded in getting a clear view of the living human retina."

2. Koenigsberger, L.: Hermann von Helmholtz, Braunschweig, F. Vieweg & Sohn, 1903.



HERMANN LUDWIG FERDINAND von HELMHOLTZ
1821-1894

PRODUCTION OF CATARACT IN RATS BY BETA-TETRALOL AND OTHER DERIVATIVES OF NAPHTHALENE

O. GARTH FITZHUGH, Ph.D.
WASHINGTON, D. C.
AND
WILHELM H. BUSCHKE, M.D.
BALTIMORE

SINCE Bouchard's [1] discovery in 1886 that naphthalene produced cataract in rabbits, a large number of experimental papers have been published on the subject. Relatively few authors, however, have attempted to approach the mechanism of this production of cataract by studying the cataractogenic properties of chemically related substances. Kolinski [2] failed to produce cataract with nitronaphthalene, β-naphthol and anthracene. Salffner [3] had negative results with 1,5-dioxynaphthalene, 2,3-dioxynaphthalene and 2,7-dioxynaphthalene. He found the cataractogenic properties of naphthalene greatly enhanced by phthalic acid; however, control experiments with other agents which likewise produced renal damage led him to conclude that the effect was a result of damage to the kidney, producing a delayed excretion of naphthalene or a toxic derivative. Igersheimer and Ruben [4] reported negative results with both α- and β-naphthol, while van der Hoeve [5] produced cataracts in rabbits with β-naphthol. Jess [6] observed occasional fine reversible clefts and opacities in the lens in cases of severe

From the Division of Pharmacology, Food and Drug Administration, Federal Security Agency, Washington, D. C., and the Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine.

1. Bouchard, A.: Production artificielle de la cataracte, Rev. gén. d'opht., 1886, p. 370.

2. Kolinski, J.: Zur Lehre von der Wirkung des Naphthalins auf des Auge, und über den sogenannten Naphthalinstar, Arch. f. Ophth. **35**:25-51, 1889.

3. Salffner, O.: Zur Pathogenese des Naphthalinstars, Arch. f. Ophth. **59**: 520-552, 1904.

4. Igersheimer, J., and Ruben, L.: Zur Morphologie und Pathogenese der Naphthalinveränderungen des Auges, Arch. f. Ophth. **74**:467-488, 1910.

5. van der Hoeve, J.: Ueber die schädliche Einwirkung des Beta-Naphthols in therapeutischen Dosen auf des menschliche Auge, Arch. f. Ophth. **53**:74-78, 1901.

6. Jess, A., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol 5, p. 270.

intoxication with quinoline. Basile [6a] observed opacities in the cortex of the lens of rabbits after repeated daily peroral administration of 0.2 to 0.4 cc. of decalol or tetralol; the changes in the lens were seen between eleven days and four weeks after onset of treatment. Chorioretinal lesions occurred, too.

In the experiments to be reported here, several chemical derivatives of naphthalene were found to be cataractogenic in rats. Although these

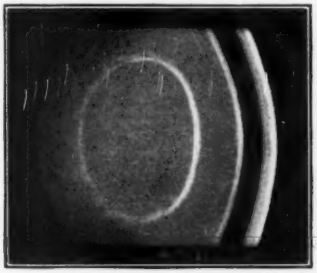


Fig. 1.—Optical section of the anterior segment of the eye of a rat fed a diet containing 2 per cent β-tetralol for two and one-half weeks.

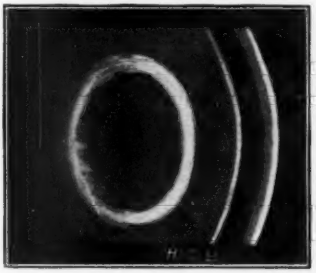


Fig. 2.—Optical section of the anterior segment of the eye of a rat fed a diet containing 2 per cent β-tetralol for four weeks.

experiments do not provide any positive evidence of the mechanism of production of this cataract, they do show that other compounds are more potent as cataractogenic agents than naphthalene. A brief report of the toxic effects of β-tetralol (1,2,3,4-tetrahydro-β-naphthol),

6a. Basile, G.: Sull azione di alcuni prodotti di idrogenazione della naftalina (tatralina e dalina) sul cristallino e membrane profonde oculari del coniglio, Boll. d'ocul. **18**:951-957, 1939.

which was proposed as an insect repellent,[7] has been made by one of us.[8] In the study of β-tetralol, over 200 rats were used, with dosage levels of 0.125, 0.25, 0.5, 1 and 2 per cent in the diet. Both weanling and adult rats were employed.

EYES OF RATS FED β-TETRALOL

Cataracts were observed in all rats with dosage levels of 0.25 per cent or more in the diet. Both the severity and the time of development of the cataracts depended on the dosage level. Cataracts could be seen grossly within three weeks in all rats given diets containing 1 and 2 per cent β-tetralol. In order to see the cataracts in the rats with lower dosage levels and at earlier stages, the slit lamp had to be used. The rats given the diet containing 0.125 per cent β-tetralol were observed for six months, without the development of cataracts.

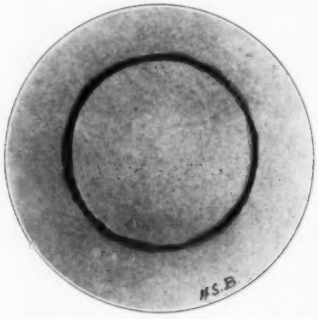


Fig. 3.—Diascopic appearance of the lens of a rat fed a diet containing 2 per cent β-tetralol ("lens in lente") for four weeks.

The eyes of the rats were examined in mydriasis with the slit lamp and the ophthalmoscope at intervals of one-half week during the first month after institution of the diet, and later at longer intervals.

Changes in the lenses visible with the slit lamp began to appear regularly between two and two and one-half weeks after beginning ingestion of the diet containing 2 per cent β-tetralol. These manifestations began with a very fine, sometimes incomplete, supranuclear haziness, which soon developed into a complete perinuclear layer showing an increased Tyndall phenomenon (fig. 1). A complete thin perinuclear shell was regularly present three weeks after institution of the diet. After four weeks this shell layer appeared somewhat denser with the

7. Jachowski, L. A., and Pijoan, M.: Two New Effective Insect Repellents NMRI-201 and NMRI-448, Science **104**:266-269, 1946.

8. Fitzhugh, O. G.: Production of Cataracts in Rats with Beta-Tetralol, Federation Proc. **5**:178, 1946.

slit lamp (fig. 2), and occasionally the deep suture lines were slightly opaque; both the superficial cortex and the nucleus, however, remained clear. At this and at later stages, on examination with the ophthalmoscope, one could see a "lens in lente" with the fundus still visible even in the axial region (fig. 3). At the end of three and one-half months a second shell had formed in the cortex, the deeper shell now being thicker and yellow in appearance (fig. 4). At this stage the fundus still was visible, in spite of the presence of the double ring opacity, but appeared somewhat blurred.

In some rats the eyes were examined four months after discontinuation of the diet containing β-tetralol, which previously had been administered for two months. In these rats the clear cortical layer outside the perinuclear opaque shell was decidedly thicker than that in the rats which had been observed at one-half week intervals continually for one month while receiving the diet containing β-tetralol. This indi-

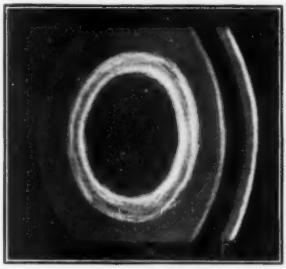


Fig. 4.—Optical section of the anterior segment of the eye of a rat fed a diet containing 2 per cent β-tetralol for three and one-half months.

cates that no permanent irreversible damage to the lenticular epithelium was produced even by prolonged β-tetralol poisoning. The epithelium of the lens appeared to continue to proliferate (or to resume proliferation) and to appose healthy lens cortex after discontinuation of the drug. In these rats the nuclear suture lines were sometimes either opaque or somewhat gaping. Lenses removed from rats killed after receiving the experimental diet about a month showed a brownish nucleus, which had a harder, drier and more brittle consistency than that of normal animals.

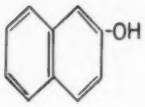
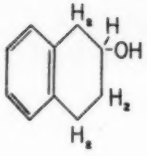
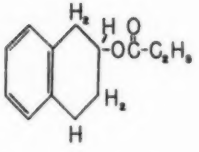
All these changes are essentially identical with those described by Goldmann [9] for rats fed naphthalene. No other ocular changes were noticed; in particular, there was no pathologic vascularization of the cornea.

9. Goldmann, H.: Experimentelle Supranuclaerkatarakt und Kernsklerose, Klin. Monatsbl. f. Augenh. **83**:433-438, 1929.

EYES OF RATS TREATED WITH OTHER DERIVATIVES OF NAPHTHALENE

In addition to the β-tetralol, the following derivatives of naphthalene were studied for their possible cataractogenic property: 1,2,3,4-tetrahydro-2-naphthyl propionate, 2-methoxy-1,2,3,4-tetrahydronaphthalene,

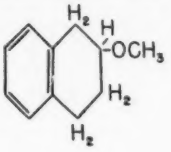
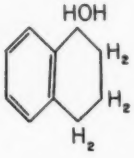
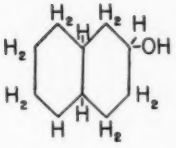
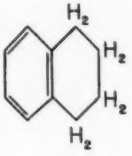
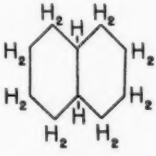
Relative Cataractogenic Property of Derivatives of Naphthalene

Name	Structural Formula	Estimated Cataractogenic Potency Compared to That of Naphthalene, Expressed as 1
Naphthalene		1
β-naphthol		1
β-tetralol		4
1, 2, 3, 4-tetrahydro-2-naphthylpropionate		4

α-tetralol, β-naphthol, trans-β-decalol (decahydronaphthol), tetrahydronaphthalene, decahydronaphthalene, β-naphthylacetate, α-naphthylacetate, β-naphthylsalicylate, β-naphthylbenzoate, α-naphthylbenzoate, β-naphthylmethyl ether, α-naphthylmethyl ether, β-naphthylethyl ether, β-methylnaphthalene, β-acetonaphthone, naphthalene-β-sulfonylchloride, β-naphthoic acid, α-naphthoic acid, β-naphthylamine and α-naphthyl-

amine. A 2 per cent concentration of each substance was incorporated in the diet and fed to 5 weanling rats for at least two months. These sub-

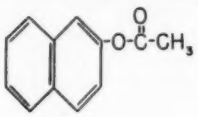
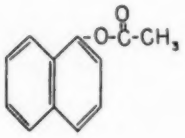
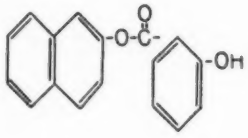
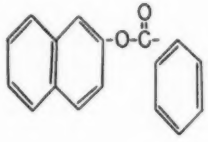
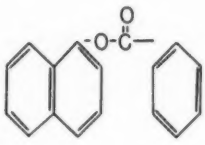
Relative Cataractogenic Property of Derivatives of Naphthalene—Continued

Name	Structural Formula	Estimated Cataractogenic Potency Compared to That of Naphthalene, Expressed as 1
2-methoxy-1, 2, 3, 4-tetrahydronaphthalene		1
α-tetralol		0
Trans-β-decalol		0
Tetrahydronaphthalene		0
Decahydronaphthalene		0

stances were compared as cataractogenic agents both with β-tetralol and with naphthalene (table).

1,2,3,4-tetrahydro-2-naphythylpropionate, 2-methoxy-1,2,3,4-tetrahydronaphthalene, β-naphthol, β-naphthylsalicylate, β-naphthylmethyl

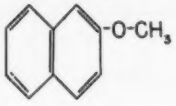
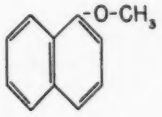
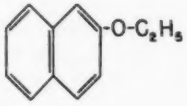
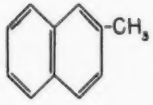
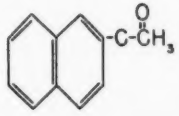
Relative Cataractogenic Property of Derivatives of Naphthalene—Continued

Name	Structural Formula	Estimated Cataractogenic Potency Compared to That of Naphthalene, Expressed as 1
β-naphthylacetate		0
α-naphthylacetate		0
β-naphthylsalicylate		4
β-naphthylbenzoate		0
α-naphthylbenzoate		0

ether and β-naphthylethyl ether produced cataracts in all rats. The 1,2,3,4-tetrahydro-2-naphthylpropionate and the β-naphthylsalicylate produced cataracts as quickly as the β-tetralol. The other substances

took much longer to produce the same degree of cataract formation and were closely comparable to naphthalene as cataractogenic

Relative Cataractogenic Property of Derivatives of Naphthalene—Continued

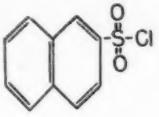
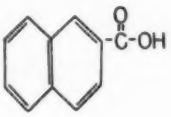
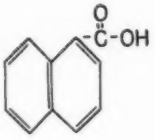
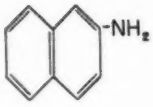
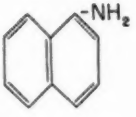
Name	Structural Formula	Estimated Cataractogenic Potency Compared to That of Naphthalene, Expressed as 1
β-naphthylmethyl ether		1
α-naphthylmethyl ether		0
β-naphthylethyl ether		1
β-methylnaphthylene		0
β-acetonaphthone		0

agents. All the cataracts appeared to be of the same type. The eyes of the rats which had been fed 1,2,3,4-tetrahydro-2-naphthylpropionate were examined with an ophthalmoscope. They showed changes in the lens similar to those described for the rats treated with β-tetralol.

ATTEMPT TO PREVENT THE FORMATION OF β-TETRALOL CATARACT

Since naphthalene is excreted in rats as a mercapturic acid,[10] it appeared possible that the derivatives of naphthalene produced cataract

Relative Cataractogenic Property of Derivatives of Naphthalene—Continued

Name	Structural Formula	Estimated Cataractogenic Potency Compared to That of Naphthalene, Expressed as 1
Naphthalene-β-sulfonyl chloride		0
β-naphthoic acid		0
α-naphthoic acid		0
β-naphthylamine		0
α-naphthylamine		0

10. Stekol, J. A.: Studies on Mercapturic Acid Synthesis in Animals: D. The Effect of Naphthalene on the Growth of Rats as Related to Diets of Varying Sulfur Content, J. Biol. Chem. **121**:87-91, 1937.

by binding essential sulfhydryl groups in the lens. Experiments with 2, 3-dimercaptopropanol (BAL), methionine, cystine and high protein diets did not support this theory. A large number of rats were treated with BAL, both by local application to the eye and by parenteral injection. The dosage levels of BAL were 3 mg. per kilogram of body weight given twice weekly for the parenteral injections and 0.01 cc. of a 5 per cent ointment placed in each eye daily for the local applications. The treatment with BAL was continued until cataracts appeared. In all instances the treatment with BAL had no effect either on the rate of development or on the severity of the cataracts. Neither a 50 per cent protein diet nor the addition of methionine equivalent to 100 mg. daily to the diet of each rat had any effect on the production of cataracts in rats fed 2 per cent β-tetralol. After a diet containing 1 per cent cystine had shown no effect on the production of cataract with 2 per cent β-tetralol, a diet containing 3 per cent cystine and 0.2 per cent β-tetralol was fed to rats. Cataracts occurred in these rats in the same length of time that they appeared in control rats, without the added cystine.

In other experiments, 0.03 per cent riboflavin and 2 per cent ascorbic acid in the diet failed to have any effect on the production of cataracts with β-tetralol.

COMMENT

Although the changes in the lens produced by feeding β-tetralol and related naphthalene derivatives are essentially identical with those described in naphthalene poisoning in rats, the difference in potency of these substances as cataractogenic agents is considerable. β-tetralol, 1,2,3,4-tetrahydro-2-naphthylpropionate, and β-naphthylsalicylate produced decided cataracts in three weeks, whereas similar doses of β-naphthol and naphthalene in the diet produced only slight cataracts in two months. Parenteral administration of solutions of β-tetralol. β-naphthol and naphthalene in peanut oil at similar dosage levels indicated that by this route also β-tetralol was more potent than the other substances. A single injection of tetralol equivalent to the amount received daily in the diet produced death within a few minutes. One-fourth this amount injected daily produced cataract in three weeks. Similar parenteral doses of β-napthol and naphthalene had no effect. With an increase in the amount either of β-naphthol or of naphthalene to twice the dose of β-tetralol which produced pronounced cataracts, slight cataracts occurred.

These experiments indicate that derivatives of naphthalene in which an oxygen atom is attached to the β carbon atom may produce cataracts in rats. In the case of trans-β-decalol, both the naphthalene rings are completely saturated, and this fact may account for the lack of any cataractogenic property. Apparently, the β-naphthylbenzoate and the β-naphthylacetate are not metabolized like the β-naphthylsalicylate, or

are not absorbed at the same rate. The experiments with the two former substances were continued for eight months without the production of cataract; this fact does not exclude the possibility of the production of cataract with prolonged feeding to rats.

SUMMARY

Changes in the lens which were similar to those described in naphthalene poisoning in rats were produced by feeding β-tetralol.

A large number of naphthalene derivatives were studied for their possible cataractogenic property. In addition to β-tetralol, 1,2,3,4-tetrahydro-2-naphthylpropionate and β-naphthylsalicylate were more potent as cataractogenic agents than was either naphthalene or β-naphthol.

By parenteral administration, β-tetralol was more than twice as potent in cataractogenic property as was either β-naphthol or naphthalene.

The treatment of rats with sulfhydryl compounds did not prevent the formation of cataract in rats fed β-tetralol.

The slit lamp drawings were made by Mrs. Annette S. Burgess, Wilmer Ophthalmological Institute.

USE OF ANTIHISTAMINIC DRUGS IN CONTROL OF ATROPINE DERMATITIS AND CONJUNCTIVITIS

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AND
ROBERT D. KIESS, M.D.
ANN ARBOR, MICH.

PHARMACEUTICAL chemists have long attempted to produce a satisfactory substitute for atropine sulfate. The desire to synthesize a substitute cycloplegic and mydriatic not related to the atropine series has been furthered by the fact that contact dermatitis and conjunctivitis occasionally develop in patients using atropine in treatment of iridocyclitis. This reaction may reach such serious proportions that it is necessary to discontinue administration of the drug. The management of the allergic manifestations usually requires discontinuation of the atropine, with substitution of homatropine, scopolamine or duboisine and the application of cold wet compresses. These substitute drugs present two disadvantages. First, none of the drugs produces a sufficiently strong cycloplegic or mydriatic action to be effective in the treatment of acute iridocyclitis. Second, the patient who is sensitized to atropine frequently demonstrates hypersensitivity to these substitute drugs, since they too belong to the atropine series.

The absence of an adequate substitute for atropine in the treatment of acute iridocyclitis often makes it imperative that use of the atropine be continued despite its side effects. However, with the advent of the antihistaminic drugs and their proved value in treatment of extrinsic allergic states, there is now available an effective aid in the control of the serious cutaneous and conjunctival manifestations of atropine hypersensitivity.

The earliest characteristic symptom of such hypersensitivity is itching. This is usually accompanied with irritation and photophobia before any of the well known signs of erythema, edema and eczema of the skin of the lids become apparent. An increase in mucous dis-

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The various doses of the antihistaminic drugs were determined with the advice of J. H. Sheldon, M.D., Chief of the Division of Allergy, Department of Internal Medicine, University of Michigan.

The diphenhydramine (benadryl®) solution used was supplied by Parke, Davis & Company, Detroit; the tripelennamine (antistin®) solution, by Ciba Pharmaceutical Products, Inc., Lafayette Park, Summit, N. J.

charge, together with chemosis and increased hyperemia of the conjunctiva, makes an early appearance. The conjunctiva commonly presents follicular hypertrophy.

The following treatment has given gratifying results in the control of atropine hypersensitivity: (1) general medication, consisting in administration of tripelennamine hydrochloride (pyribenzamine hydrochloride®; N,N-dimethyl-N′-benzyl-N′-[α-pyridyl] ethylenediamine hydrochloride), 50 mg. by mouth four times a day: (2) local application of solution of diphenhydramine hydrochloride (benadryl hydrochloride®), 0.5 or 0.25 per cent,[1] four times a day. In all cases atropine sulfate (1 per cent) was continued in order that the mydriasis might be maintained.

This paper presents the reports of treatment in 9 consecutive cases of atropine sensitivity. The results, both objective and subjective, in these cases were evaluated as "excellent," "good," "fair" and "poor."

REPORT OF CASES

Case 1.—J. W., a white man aged 63, exhibited the classic signs and symptoms of atropine dermatitis and conjunctivitis on the third day after intracapsular cataract extraction with peripheral iridectomy in the left eye. He had been receiving instillations of atropine sulfate (1 per cent) once daily in the left eye for five days. His symptoms were intense itching and irritability. Objective signs were pronounced injection of the conjunctival vessels, mild chemosis, eczema, erythema and edema of both lids. The suggested therapeutic regimen was initiated, and within forty-eight hours there was "excellent" relief from the symptoms and the decrease in signs was noted as "good."

This plan of therapy was continued for eleven days, during which time there was little change in the symptoms and signs.

Case 2.—J. H., a white man aged 65, exhibited the typical signs and symptoms of atropine dermatitis and conjunctivitis on the third day after intracapsular cataract extraction with peripheral iridectomy in the right eye. He had been receiving atropine sulfate (1 per cent) in the right eye daily for four days. Therapy was carried out as outlined. Within forty-eight hours relief from symptoms was recorded as "good" and decrease in signs as "fair."

Treatment was continued for one week, with no essential change.

Case 3.—C. G., a white man aged 45, exhibited the usual signs and symptoms of atropine dermatitis and conjunctivitis on the fourth day after iridectomy for acute glaucoma. He had been receiving atropine sulfate (1 per cent) once daily for two days in the surgically treated eye. The suggested therapeutic regimen was begun, and within forty-eight hours "excellent" symptomatic relief and a "good" response in clinical signs were observed.

Case 4.—H. N., a white man aged 53, exhibited atropine dermatitis and conjunctivitis on the fourth day after bilateral iridectomy for glaucoma secondary to uveitis. Atropine sulfate (1 per cent) had been used once daily in

1. At present, a 0.25 per cent solution of diphenhydramine hydrochloride is being used.

both eyes for two days. The suggested therapeutic regimen was initiated. "Excellent" relief from symptoms and a "good" response in clinical signs were observed in forty-eight hours.

CASE 5.—S. A., a white man aged 55, with retinal separation in the left eye, had been treated with bed rest and pinhole glasses and mydriasis obtained with use of atropine sulfate (1 per cent) once daily, for preoperative study. After two days of medication with atropine, dermatitis and conjunctivitis of the left eye developed. The treatment suggested for control of atropine sensitivity was initiated, with "excellent" symptomatic relief and "good" response in signs within forty-eight hours. At this time diathermy was performed for correction of the retinal detachment. Two days after operation the atropine dermatitis and the conjunctivitis of the left eye recurred. It was found, however, that the patient had not received his antihistaminic medication after operation, and the treatment was reordered. Within forty-eight hours the relief from symptoms was "excellent" and the decrease in signs was "good." It should be noted that the patient's clinical responses on the two occasions were similar.

CASE 6.—F. G., a white woman aged 67, exhibited atropine dermatitis and conjunctivitis on the fifth day after intracapsular cataract extraction with peripheral iridectomy in the left eye. Atropine sulfate (1 per cent) had been instilled daily in the left eye since the operation. Medication consisted in administration of tripelennamine hydrochloride (50 mg.) by mouth four times daily and instillation of antistin® solution (2-[n-phenyl-n-benzyl-aminomethyl]-imidazolin), 0.5 per cent, into the left eye four times daily. Within forty-eight hours the relief from symptoms was "good" and the decrease in signs "fair." There was no further change after ten days of this treatment.

CASE 7.—M. M., a white woman aged 34, exhibited severe atropine dermatitis and conjunctivitis fourteen days after discission for congenital cataract of the right eye. She had been receiving atropine sulfate (1 per cent) daily in the eye operated on. Antistin® was used locally four times a day in 0.5 per cent concentration, with the atropine sulfate.

Observation after four days revealed that the signs and symptoms had considerably increased. Medication was then changed to oral use of tripelennamine and local instillation of diphenhydramine, as indicated earlier in the paper. The patient was observed for two weeks while receiving this medication, and both symptomatic relief and decrease in signs remained consistently "poor." All medication was then discontinued, since relief from antihistaminic drugs was not obtained.

CASE 8.—B. T., a white youth aged 19, had sustained severe corneal burns from sodium aluminate. A complicating bilateral iritis was being treated with instillations of atropine sulfate (1 per cent) once daily in each eye. After ten days of atropine therapy, dermatitis and conjunctivitis developed. The suggested therapeutic combination of diphenhydramine and tripelennamine was given. After forty-eight hours relief of symptoms was "excellent" and decrease in objective signs "good."

CASE 9.—B. M., a white woman aged 58, exhibited atropine dermatitis and conjunctivitis on the third day after intracapsular cataract extraction with peripheral iridectomy in the left eye. Instillation of atropine sulfate (1 per cent) had been given the night before operation and was continued at the daily dressings. The usual therapy was ordered. Within forty-eight hours "excellent" symptomatic relief and "good" response in clinical signs were obtained. This therapeutic regimen was continued, and an intracapsular cataract extraction with peripheral

iridectomy was performed on the right eye one week after the extraction in the left eye. Postoperative orders were written specifically to continue the systemic administration of tripelennamine, and diphenhydramine therapy was maintained only for the left eye. There was no change in the clinical findings in the left eye. Two days after cataract extraction was performed on the right eye, atropine dermatitis and conjunctivitis in the surgically treated eye developed, despite the oral administration of tripelennamine. The patient had been receiving atropine sulfate (1 per cent) daily in the right eye for three days. Instillations of diphenhydramine hydrochloride, in 0.5 per cent solution four times a day, in the right eye was added to the therapeutic regimen. Within forty-eight hours the relief from symptoms was "excellent" and the decrease in signs "good."

SUMMARY AND CONCLUSIONS

From these consecutive cases, the following general conclusions may be drawn:

1. Atropine sulfate may be continued after the development of atropine dermatitis and conjunctivitis, since the reaction is controllable by concurrent antihistaminic therapy.

2. Pronounced improvement with antihistaminic treatment was noted within forty-eight hours in 8 of 9 consecutive cases of atropine hypersensitivity.

3. In two thirds of the cases reported, relief from symptoms was "excellent" and the decrease in clinical signs was "good."

4. A combination of local and general antihistaminic therapy proved most effective. This finding was most apparent in a case in which atropine hypersensitivity developed during systemic administration of tripelennamine alone, while in another case the result was poor when treatment was limited initially to local application of an antihistaminic substance.

5. From this limited series, it would seem that the treatment of choice is a combination of oral administration of tripelennamine hydrochloride and local use of diphenhydramine hydrochloride. The limitations of instillation of a solution into the conjunctival cul-de-sac in the control of reactions of the skin are obvious. Further studies are being conducted with the application of an ointment containing 2 per cent tripelennamine hydrochloride to the involved areas of the skin.

University Hospital.

CHOROIDAL METASTASIS OF A TESTICULAR CHORIONIC EPITHELIOMA

Report of a Case

GEORGE K. KAMBARA, M.D.
LOS ANGELES

METASTASIS of chorionic epithelioma to the choroid is rare. Six cases have been reported in the literature, 3 of occurrence in women and 3 in men. Our case is the seventh one to be reported, and the fourth of occurrence in a man.

The first report of a case of chorionic epithelioma with metastasis to the choroid was made by Mulock-Houwer [1] in 1926. A woman had metastases to the choroid, lung, kidneys and intestine three years after an abortion. The uterus was enlarged. The second report, by Slavik [2] in 1933, was the case of a woman aged 50 who had had a supravaginal hysterectomy for hydatidiform mole. She had had an attack of acute glaucoma, for which enucleation was performed. A metastasis was noted in the choroid. Two weeks later the patient died with cerebral metastases. Simidu [3] reported the third case in 1935. A woman aged 31 had chorionic epithelioma of the uterus. She also had malignant glaucoma with pain and blindness, requiring enucleation of the left eye. The typical tumor cells were observed in the choroid. There was associated retinal detachment.

In 1936, MacDonald [4] reported the first occurrence of choroidal metastasis from a testicular chorionic epithelioma. A man aged 28 had noted a slowly increasing mass in the left testicle for eight months. Hemoptysis and epistaxis occurred a few months before the loss of vision. Retinal detachment was seen in the right eye, with an underlying visible mass. Enucleation was performed because of the pain and increased tension. Typical cells of chorionic epithelioma were

From the Department of Ophthalmology of the University of Wisconsin Medical School, Dr. F. A. Davis, Chairman.

1. Mulock-Houwer, A. W.: Metastasis of Malignant Chorio-Epithelioma, Klin. Monatsbl. f. Augenh. **77**:226, 1926.

2. Slavik, B.: Metastasis of Malignant Chorionepithelioma into Choroid, Časop. lék. česk. **72**:756, 1933.

3. Simidu, S.: Metastase eines malignen Chorioepithelioms in der Aderhaut, Acta soc. ophth. jap. **39**:2023, 1935.

4. MacDonald, A. E.: Choroidal Chorionepithelioma Secondary to Teratoma of Testicle, Arch. Ophth. **16**:672 (Oct.) 1936.

observed in the choroid. Metastases were present in the lung, in subcutaneous tissues of the groin, in the skull, brain, nasopharynx, pleura, diaphragm, liver, gallbladder, intestine and kidneys and in the retroperitoneal tissues. The patient also had signs of associated endocrine changes—linea nigra, female distribution of pubic hair and hypertrophy of the breasts.

Reichling [5] presented a case in 1938 in which the eye was enucleated because of a suspected malignant melanoma of the choroid. However, it was demonstrated later that the growth was a metastasis from a tumor of the right testis. The patient died of generalized metastases within two months. Typical tumor cells were observed in the choroid. This report was not complete.

In 1944 Godtfredsen [6] reported the third case of choroidal metastasis in men and presented a review of the previous cases and the biologic and histopathologic characteristics of the tumor. A youth aged 18 had been aware of increasing swelling of the right side of the scrotum for a year. Two months prior to admission aspiration and injection were carried out for cure of the hydrocele. However, there was no improvement, and later semicastration was performed. The diagnosis of chorionic epithelioma was then made. He later noted impairment of vision, and a choroidal tumor was seen superiorly and temporally in the right eye. His general condition became poor, and he died two weeks after admission. Metastases were observed in the cerebrum (cortex), lungs, liver, pancreas, jejunum and skin. The hypophysis showed none of the changes seen in association with pregnancy.

REPORT OF CASE

E. B., a man aged 21, was admitted to the Wisconsin General Hospital on Feb. 17, 1947, with the complaint of pain in the right side of his chest. He had been well until November 1946, when there developed a dry cough which was not associated with a cold. This cough persisted into the latter part of December. He then experienced pleuritic pain in the right side of the chest. He began to raise about one-half cup of bloody sputum a day. He noted at this time that the left testis was considerably larger than the right, but it was not painful.

Ten days prior to his admission the left testis became painful, and his right eye felt swollen and began to water. Shortly afterward he noted blurring of vision, and two days prior to admission he was seen at the Davis and Neff Clinic. A small, well demarcated elevation of the retina was noted above and temporal to the disk. The following day the patient had severe pain on both sides of his chest and was admitted for complete study.

5. Reichling, W.: Ocular Metastasis of a Chorionepithelioma, Arch. Ophth. **19**:156 (Jan.) 1938.

6. Godtfredsen, E.: Choroid Metastases in Chorionepithelioma of the Testicle, Acta ophth. **22**:300, 1944.

The appetite had been poor for two weeks. He also had nocturia, urinating two or three times during the night. He had noted severe generalized weakness. He had lost 8 pounds (3.6 Kg.) in weight.

The past history was noncontributory. His social and family histories were not remarkable.

On examination the patient appeared well developed and fairly well nourished but in apparent distress. There was pallor of the skin, lips and mucous membranes. The anterior cervical lymph nodes were palpable bilaterally. The trachea was deviated slightly to the left. A large, firm, nodular, movable mass, measuring 3 by 3 cm., was felt under the right breast, and a smaller mass was palpable under the left breast. The expansion of the chest was decreased bilaterally. There was dulness over the right side, with decrease to absence of breath

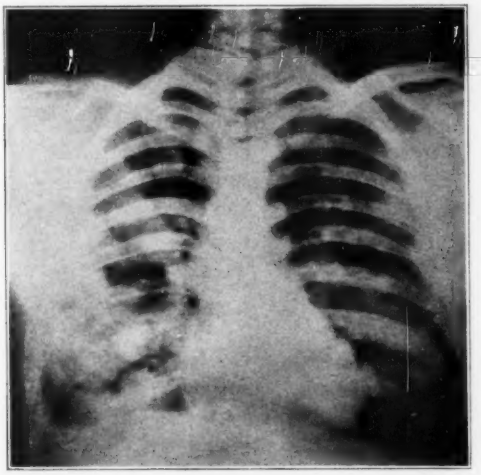

Fig. 1.—Roentgenogram of the chest, showing multiple nodular metastases to both lungs.

sounds. Rales were heard throughout the chest. The heart and mediastinum were shifted to the left. The pulse rate was 108 per minute, and the blood pressure 114 systolic and 68 diastolic. The abdomen was tense, and the edge of the liver was felt to extend 8 to 10 cm. below the costal margin. The surface of the liver was nodular.

The left testis was enlarged, nodular, tender and firm; it measured 5.5 cm. in diameter. The head of the epididymis appeared unaffected. Two firm, tender nodules were attached to the vas deferens, or spermatic cord, just above the epididymis, one being 0.5 cm. and the other 2 cm. in diameter. The right testis was normal. The prostate gland was slightly enlarged, but very tender.

There were no neurologic signs.

I made an ocular examination on Feb. 18, 1947: Vision was 6/200 in the right eye and 20/15 in the left eye. The extraocular movements were good.

There was no injection of the right globe or any proptosis or palpable masses about the eye. The right pupil was at 3 mm. and the left 2.5 mm. in diameter. Both pupils reacted to light and in accommodation. The anterior chambers had normal depth. Tension in the right eye was 10 mm. of mercury (Schiøtz) and that in the left eye 13 mm.

Funduscopic examination of the right eye on February 19 showed that the media were clear. The disk had good color and a central cup of medium size. In the superior part of the temporal field there was a dark gray, elevated mass, which extended to the level of the macula inferiorly, to the meridian of the disk nasally and toward the superior temporal periphery; it covered an area about eight times the size of the disk. This mass was elevated about 10 D. Along the inferior border the macular fibers of Henle were seen in bold relief. In

Fig. 2.—Photograph of the fundus of the right eye taken on Feb. 25, 1947, showing the elevated mass under the retina and the hemorrhages, with light centers.

the center of the elevated area, and somewhat superiorly and temporally, were yellow-white patches and irregular hemorrhages. In the superior temporal periphery, about 7 disk diameters from the disk, there was a pigmented area about half the size of the disk, in the center of which a hole was seen in the retina. Slightly inferior and nasal to this hole was the operculum. In the inferior half of the fundus, beginning about 3 disk diameters from the disk, there was a serous detachment of the retina, which was elevated about 4 D. This detachment did not extend to the inferior temporal periphery. The left fundus appeared entirely normal.

The impression was that of metastatic tumor of the choroid of the right eye with associated retinal detachment and hole.

The clinical diagnosis was primary neoplasm of the left testis, probably a teratoma or chorionic epithelioma, with metastases to the gastrointestinal tract, to both lung fields, to the right eye and to both breasts.

Laboratory Studies.—The urine was normal.

Routine studies of the blood showed 9.8 Gm. of hemoglobin, with 3,160,000 red blood corpuscles per cubic millimeter. The white cell count was 11,100, with 72 per cent polymorphonuclear leukocytes (of which 57 per cent were filamentous and 15 per cent nonfilamentous forms), 25 per cent lymphocytes and 3 per cent monocytes. The sugar and nonprotein nitrogen of the blood were within normal limits. The Wassermann reaction of the blood was negative. The sedimentation rate was increased to 35 mm. in one hour, corrected (Wintrobe).

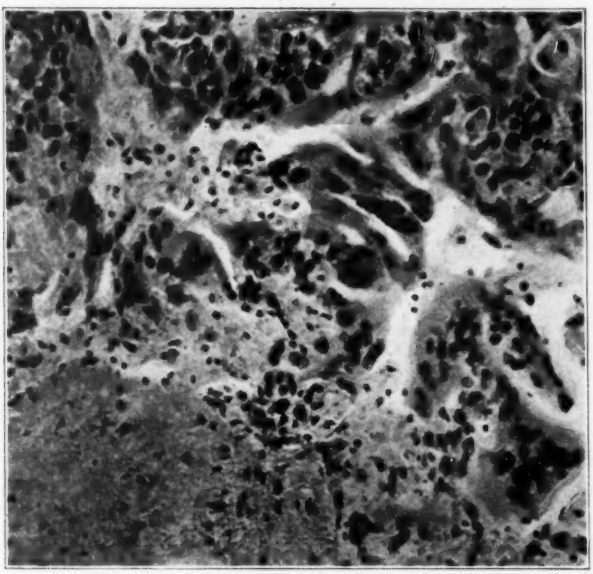

Fig. 3.—Langhans and syncytial cells in a metastatic nodule in the kidney; × 175.

Roentgenograms of the skull showed no evidence of metastasis involving the cranial bones. The arms and thighs revealed no metastases. Roentgenograms of the chest (fig. 1) showed both pulmonary fields to be riddled with nodular shadows, sharply circumscribed and ranging in size up to 4 cm. in diameter. There was a slight pleural reaction at the base of the right lung, with a small amount of fluid. The left pleural cavity was free of fluid. The size and shape of the heart were normal.

The Mantoux test gave a negative reaction to 0.01 mg. of old tuberculin U. S. P. in forty-eight hours. Cultures of aspirated gastric contents did not yield tubercle bacilli.

The quantitative Aschheim-Zondek test showed 4,000 rat units per liter of urine, a value which was very high.

On February 19 thoracentesis was performed through the ninth intercostal space on the right side, between the midscapular line and the axillary line, with removal of 850 cc. of bloody fluid. The fluid appeared like venous blood but did not clot on standing. Analysis of the fluid showed 7.6 Gm. of hemoglobin and 2,660,000 red blood cells and 8,250 white blood cells per cubic millimeter. The cultures yielded no organisms in forty-eight hours.

On February 20, biopsy of the mass in the right breast and of a lesion over the left costal margin was performed by the surgical resident, Dr. Thuerer,

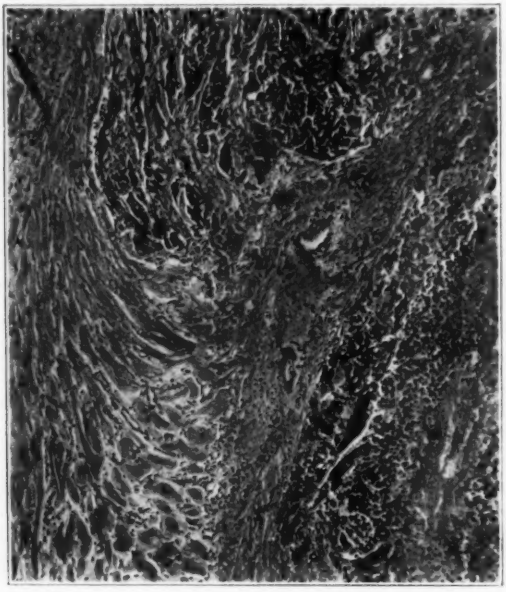

Fig. 4.—Metastases to the heart muscle; × 80.

with use of local anesthesia. The report of this biopsy, by Dr. W. Jaeschke, was as follows:

"The sections showed partly necrotic and hemorrhagic tumors, composed of broad bands and irregular masses of tumor cells. Most of the cells were closely packed and moderately vacuolated and had good-sized, oval to round reticular nuclei. Mitotic figures were fairly common. Some of the cells were not clearly defined and were arranged in irregular syncytial masses of various sizes. In some cells the cytoplasm stained blue and in others pink.

"The impression was that of metastatic chorionic epithelioma."

I examined the fundus every other day. The dark, elevated mass continued to enlarge during the period of observation. It extended nasally beyond the

meridian of the optic disk and inferiorly 1 disk diameter below the level of the fovea. It also became more elevated and was seen with a +12 lens in the ophthalmoscope. New flame-shaped hemorrhages were seen on each examination. Some of these had light centers. The serous detachment in the lower part of the fundus increased in extent steadily and, when seen just prior to the patient's death, was elevated 6 D.

During the patient's course in the hospital the intraocular tension was always lower in the involved eye. The only change seen in the left eye was the pallor of the optic disk, associated with the severe anemia.

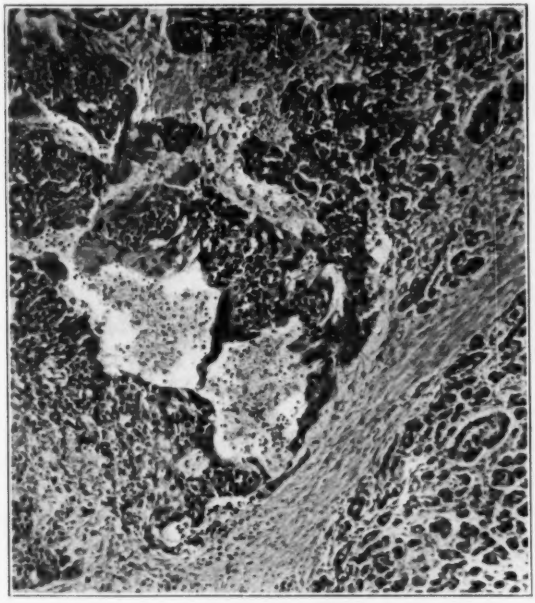

Fig. 5.—Metastatic nodule in pancreas, showing typical Langhans and syncytial cells to the left and compressed pancreas to the right; × 80.

An attempt was made to take photographs of the fundus; but, because of the high elevation and the poor condition of the patient, the results were not satisfactory. One photograph is reproduced (fig. 2).

The general course of the illness was rapidly downhill. The patient required injections of morphine for relief of the pain in the right eye and chest. He died on February 27, ten days after admission.

Necropsy.—Autopsy was performed thirteen and one-half hours after death. A summary of the findings taken from the complete report made by Dr. Ralph C. Frank, of the department of pathology, follows: The pleural surfaces were studded with innumerable tumor nodules, of all sizes. Cut sections of the lung showed that all portions were involved by round, hemorrhagic and gelatinous

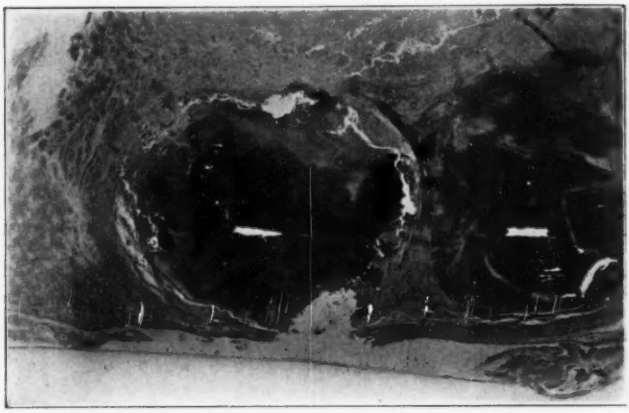

Fig. 6.—Left testis, showing primary tumor with large areas of hemorrhage; × 4. Compressed testicular tissue at the left side shows spermatogenesis.

Fig. 7.—Metastatic nodule to brain just under the meninges; × 23.

nodules. The hilar nodes were enlarged and involved by tumor. A small hemorrhagic nodule was observed in the posterior wall of the left ventricle and another below the aortic orifice in the endothelium. Multiple metastatic nodules were seen under the capsule of the spleen and in cross sections of the organs. Similar areas were seen in the liver. The gallbladder was not involved. The stomach had small metastases along the greater curvature. A large nodule

Fig. 8.—Metastases to the choroid of the right eye, extending to the disk; × 5½. A serous detachment of the retina has occurred on the other side of the disk and over the tumor.

almost occluded the esophageal opening at the cardia. Three nodular areas were noted in the jejunum, but the large bowel and rectum were free from tumor. Multiple lesions were seen in the pancreas. The right adrenal gland had nodules in the medullary spaces and cortex. Both kidneys had multiple

nodules under the capsule, being more numerous in the right kidney. The ureters contained no metastases. The prostate gland and seminal vesicles appeared normal. The right testis was normal, but the left was completely replaced with hemorrhagic tumor tissue. There was an area of tumor tissue just above the left testis in the spermatic cord. The thyroid was normal.

Microscopic Examination.—The tumor tissue had an extremely malignant appearance, with great variations in the size, shape and chromaticity of the nuclei. Mitotic figures were frequently seem. The typical cells had round or

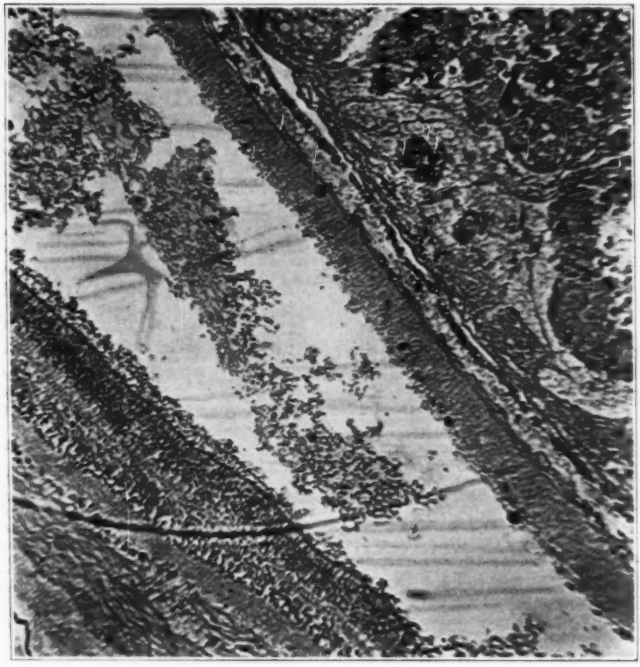

Fig. 9.—Metastasis to the choroid of the right eye (right side); × 90. Serous detachment of the retina has occurred over this nodule; the separation is within the layer of rods and cones.

ovoid nucleoli (fig. 3). Other types had darker nuclei. The cytoplasm was basophilic, but for the most part was poorly demarcated, and frequently syncytia of cells were seen in which only the nuclei were distinct and the cell borders were completely lost. Necrosis and hemorrhages were of frequent occurrence in the various sections. The nodules containing the typical cells were seen in the heart (fig. 4), lungs, spleen, liver, pancreas (fig. 5), submucosa of the stomach and jejunum, cortex and medulla of the right adrenal gland and both kidneys. The left testis showed spermatogenesis in the remaining testicular tissue, but the

major part of the section was replaced with necrotic tumor cells and large hemorrhagic areas (fig. 6).

The right testis showed normal spermatogenesis and had no tumor. The left breast showed no metastases but was hyperplastic, with increased activity of the glandular epithelium. The pituitary glands showed no apparent pathologic process. The thyroid was normal.

The brain was studied separately by Dr. Richard Retter, of the department of pathology. Three distinct hemorrhagic nodules overlay the left occipital pole and the left parietal region. On cut section a nodule was seen in the left frontal lobe. On microscopic sections metastatic nodules were seen underlying the meninges (fig. 7). There was localized thickening of the meninges over the nodules. Surrounding the nodules were shrinking and pyknosis of the neurons and moderate increase in glial elements.

I removed the right eyeball at the time of autopsy, or about fourteen hours after death, and fixed it in Zenker's solution. The report from the laboratory of ophthalmic pathology was made by Dr. Peter Duehr. Grossly, the tumor measured 5 by 10 mm. The retina was detached over the tumor mass (fig. 8).

Microscopic examination (fig. 9) revealed that the eye was of average size. The interior of the eye contained a tumor occupying about one sixth of the globe. The tumor was located in the choroid, extending from the optic nerve forward to pass the equator. The main mass of the tumor was filled with blood, making study of the cells impossible. Around the periphery of the tumor the cells were well defined. The tumor cells contained large, various-sized, round to oval nuclei, which stained pink and were reticulated. The nuclei were closely packed, and the cytoplasm was sparse. Among the closely packed cells were vascular spaces, which contained only a few blood cells and much foamlike and granular, pink-staining material. Mitotic figures were common. The retina was edematous and detached. The cornea was devoid of epithelium. The anterior chamber was open. The iris and ciliary body were not remarkable. The sclera and optic nerve appeared normal.

The final diagnosis was primary chorionic epithelioma of the left testis, with metastases to the spermatic cord, kidneys, right adrenal body, liver, pancreas, spleen, jejunum, stomach, heart, lungs, brain, subcutis, right choroid and right breast. There was also gynecomastia and fibrocaseous tuberculosis of the liver and spleen.

COMMENT

The case presented is, as far as we can determine, the fourth case of chorionic epithelioma with metastasis to the choroid observed in a man. The initial complaint, which brought the patient to the ophthalmologist, was failure of vision in the right eye. He had had a persistent cough, suggesting metastases to the lungs, two months previously. After the visual disturbance, the course was rapidly downhill, the patient dying within three weeks.

The origin of the tumor was in the left testis. Metastases were observed in the cerebral cortex, the choroid of the right eye, both lungs, the heart, stomach, small intestine, kidneys, liver, spleen, pancreas, the right adrenal gland, the right breast and the subcutaneous tissue. No metastases were noted in the roentgenograms of the bones. None was found in the pituitary body. The urine showed a high concentration

of estrogens. Photographs of the fundus were taken, but the results were not satisfactory because of the high elevation of the retina and tumor. One photograph is reproduced (fig. 2). The intraocular tension was lower in the eye involved. In previous reports the tension was elevated, and the eyes had to be enucleated because of glaucoma. The typical Langhans and syncytial cells were seen both in the primary tumor and in the metastases.

Of the 4 cases of testicular chorionic epithelioma with metastasis to the choroid, the right eye was involved in 3. Reichling,[5] in his incomplete report, did not specify which eye. The primary source was from the right testis in 2 cases and from the left testis in 2 cases. The patient lived two months after onset of visual disturbance in Reichling's case, one month in MacDonald's, three weeks in mine and two weeks in Godtfredsen's.

SUMMARY

A case of a testicular chorionic epithelioma with metastases to the choroid of the right eye is presented. Only 3 other cases of occurrence in men have been reported. Three cases with metastases to the choroid in women from chorionic epithelioma of the uterus have been reported.

In the present case, metastases were observed in the brain, breast, stomach, intestine, liver, adrenal gland, subcutis, heart, lungs and pancreas.

312 East First Street.

VOLUNTARY DISSOCIATION OF THE ACCOMMODATION AND THE CONVERGENCE FACULTY

Two Observations

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MANY persons have volitional control of convergence; at the command, "Cross your eyes," they are able to do so with ease. Others cannot, but after a period of tutelage they acquire the faculty. A simple exercise to bring this about consists in having the subject regard a pencil at the punctum optimum and then hold his eyes in their assumed position by "imagining" the pencil after its withdrawal, demonstrating an obviously conscious influence. This control probably can be conditioned to occupy a subconscious level, since the position can be held in the face of distracting influences and the diversion of conscious thought. A patient described by Walsh [1] had apparently developed great skill in the voluntary control of her convergence and in voluntary alternate suppression. A third group of persons is made up of those who seem quite unable to acquire volitional control of convergence. It has been demonstrated that these voluntarily induced convergences are usually accompanied with corresponding increases in the accommodation and by miosis; conversely, it is easily possible, with numerous devices, to disassociate the accommodation and the convergence. Those who experiment with ocular gymnastics often find that they can accomplish this disassociation voluntarily under certain conditions. Years ago I acquired the not uncommon ability of getting vivid stereoscopic effects with Brewster type pictures without the use of the Brewster instrument. A friend employed in aerial map making introduced me to this phenomenon. He used aerial photographs taken over rugged but familiar terrain for the demonstration. His employment duties required him to insert these slightly dissimilar pictures into a modified stereoscopic device and from the resultant three dimensional effect to create the required maps, including to some extent the regional topography. He had discovered that he could get the same effect impressed on his visual cortex without the use of the instrument, and he acquired such facility in the technic that much of his work was thereafter done unaided. The phenomenon was

1. Walsh, F. B.: Clinical Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947, p. 275.

readily identifiable as a voluntary disassociation of the accommodation and the convergence faculty, and I was able to duplicate his control promptly, with a vivid sensation of peaks and canyons resulting from the integration of his photographs. One smaller pinnacle which I had scaled a number of times afoot seemed fairly to shoot up at me from the familiar creek bed below. Since that time, unaided stereoscopy has continued to be easy with suitable material. This phenomenon is, of course, common among ophthalmologists and among roentgenologists; many of the latter learn to get a stereoscopic effect from their films unaided merely by selecting a favorable distance from their view boxes. I recount this as information preliminary to the following observation.

The observation resulted from my idly looking out a window. This window beside my desk is 24 inches (60 cm.) from my eyes as I gaze over the rooftops at an attractive distant building. The glass in this window is reenforced by embedded wire mesh, the meshes being regularly hexagonal and about 1 inch (2.5 cm.) in diameter. About 4 inches (10 cm.) beyond the reenforced glass is a stout burglar screen of another type of wire mesh, the meshes in this case being square, regular and slightly more than ½ inch (1.3 cm.) in diameter. The burglar screen was put in place because of a fire escape outside the window; the fire escape is 2 feet (60 cm.) in width and is guarded by an outer rail of slender steel bars. While gazing at the distant building (about 1 mile [1.6 kilometers] away) I became aware that the hexagonal pattern of the glass-reenforcing wire was covering my view in a curious manner. It conveyed the impression of lying about 12 inches (30 cm.) beyond the window frame; that is, it appeared as a mesh wire fence dividing the fire escape into two lanes. I fixed the impression strongly in my mind and then cautiously increased my accommodation from infinity to the illusory position of the wire pattern about 3 feet (90 cm.) away. By doing this slowly, I found myself able to bring the details of the hexagonal meshwork into sharp, optimum focus, seeing all visible details of the complex little patterns of gas bubbles embedded in the glass around the wire. I was able to scrutinize this pattern as acutely and subconsciously as though it were a sheet of newspaper 3 feet away. At this time the burglar screen (square) mesh appeared slightly blurred but seemed about 3 inches (6.3 cm.) nearer my eye than the hexagonal mesh, thus appearing to be displaced outward from its true position perhaps 9 inches (22.5 cm.). During this illusion the slightest motion of the head created multiple plane parallax shifts of these various grills, in keeping with their true positions; the parallax was therefore antagonistic to the illusory impressions, and yet the antagonism was not strong enough to disrupt the illusion.

I have repeated the optical illusion many times and find it no longer necessary to begin the experiment by focusing on the remote building (infinity). I can focus on the hexagonal mesh within the window glass (at 24 inches, or with about 1.5 D. of accommodation and 1.5 meter angles of convergence), and then, by relaxing a trifle, cause the optical illusion mesh to appear halfway across the fire escape (at 36 inches [90 cm.], or with about 1 D. of accommodation and 1 meter angle of convergence). This mesh appears somewhat blurred if all function is arrested at this point; but if the accommodation is again carefully increased to 1.5 D. and the convergence is left at 1 meter angle, the blur disappears and the wire with its little bubbles takes on normal clarity, retains its illusory position

and appears slightly magnified. If the hexagonal mesh were moved physically to a point 1 foot beyond the window frame, the mesh would appear smaller, in keeping with the law of the square of the distance; moving it psychically to this position makes it larger by an apparent 20 per cent (estimated). It is then easy to increase the accommodation slightly to clarify the burglar mesh in its illusory position, then to increase both accommodation and convergence to see the burglar mesh in its true position and, finally, to increase both accommodation and convergence still more to see the hexagonal mesh in its true position; here it appears to be about 20 per cent minified from its apparent size in the illusory position.

The ocular gymnastics per se are of little interest, and the illusion is easily explained. The hexagonal mesh is of such size that the eyes are focused on adjacent meshes in the illusory position; the gas bubble patterns serve as effective orientation marks. The cerebral picture integrated from these two almost identical meshes shows a composite, or summation, of the bubble patterns of the two meshes, or true fusion. This means that the lines of fixation of the two eyes cut corresponding points of adjacent meshes 2 feet away and intersect each other 3 feet away. The eyes, being converged to the 3 foot plane, are under about 1 meter angle of convergence. By an increase in disassociated accommodation to 1.5 D., the illusory image is clarified but does not leave its illusory plane. It seems reasonable, therefore, to assume that psychic localization of the horopter in space is predicated on the convergence faculty primarily and on the accommodative faculty secondarily or not at all.

In studies on stereoscopic accuracy in relation to the duration of the illumination, Langlands [2] found that a spark discharge of $\frac{1}{150,000}$ second's duration permitted considerable accuracy in stereoscopic localization. As the exposure time increased, the stereoscopic accuracy also increased; this increase was most rapid in tests with time intervals between 0.1 and 0.5 second. This zone of rapid increase corresponds with the action time of the ocular muscles, but Duke-Elder [3] expressed doubt that differentiations so fine are based on proprioceptive muscular impressions. While stereopsis is the summational effect of numerous contributory factors, I believe that psychic localization of the horopter is predominantly an expression of convergence, and I find it difficult to deny a place to proprioception. The deterioration of stereopsis at great distances is in keeping with the infinitesimal variations in convergence involved. The spark discharge studies of instantaneous stereopsis seem compatible with this view, as the brain is merely comparing the flash with the horopter; it is not necessary for one to shift the horopter to appreciate whether a spark lies without or within it or to estimate the distance quantitatively. The time factor thus becomes of secondary importance. It is necessary only for the spark to record itself on disparate points of the immobile retinas in order

2. Langlands, T.: J. Optic. Soc. America **28**:45 and 83, 1927; cited by Duke-Elder.[3]

3. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1944, vol. 1, p. 1078.

to establish its position in relation to that of the horopter. The position of the horopter, while constantly varying, is at any instant available for instantaneous comparisons.

In his discussion of lesions involving the posterior oculogyric mechanism, Walsh [4] mentioned the case reported by Holmes and Horrax, in which the patient, after a military head injury, sustained no paresis of the extraocular muscles but was unable to converge on a near object and lost his stereopsis. Walsh [5] quoted Adler in listing the mechanisms involved in perception of depth:

> (7) Accommodation: As each eye must be accommodated for objects nearer than infinity in order to see them clearly the amount of accommodation necessary may be of some aid in determining their position. This is a relatively unimportant factor in man, however.

This small part played by pure accommodation must be very minor. It is extraordinarily difficult to estimate the distance of a soap bubble above one against a cloudless sky with one of the eyes covered. The integration of two images for binocular depth perception introduces, among other things, the convergence factor and the dissimilarity of the images. These also can be readily separated by many means. I recently saw some three dimensional material prepared from photographs in such a manner that the topographic, or relief, effect was intentionally exaggerated through the stereoscope; the binocular resultant was startling in its stereoscopic impact, but the mean level of the picture was stable; it lay on the horopter determined by the state of the eyes and the viewing mechanism. The horopters for the various levels of the picture involved changes in convergence, but no changes in accommodation.

The increase in the disassociated accommodation during my illusion with the grills accounts for the magnification of the illusory image: but since the eye is accommodated 1.5 D. to see the true image in its true position and also 1.5 D. to see the illusory image clearly, this increase is not a real one; it is only relative to the convergence. Thus, the convergence also becomes the only variable in action to affect the image size as well. It is possible to demonstrate this on the major amblyoscope easily. Throughout the experiment the tubes are left locked after a selected position has been found. One may place a moderate burden on the accommodation, if desired, by putting —3 D. spheres in the cells of the eyepieces. Then, by trial and error, a position of relative divergence is located for the tubes in which horizontal diplopia exists but which can be overcome in a few seconds. The tubes are locked. The subject returns his eyes to the

4. Walsh,[1] p. 299.
5. Walsh,[1] p. 253.

eye pieces and experiences obvious separation of the images. By selecting a small defect or a preplaced ink dot on one of the slides (preferably for the dominant eye), the subject may suppress the other eye and accommodate to maximum acuity on the defect, and then on the whole slide. This image may be made crisp and clear, and held that way. Then, by volitional convergence control (actually, a reduction of convergence) the diplopia can be made to lessen. When the two images finally come very close to each other, they will abruptly slip together with a sudden motion and a simultaneous magnification in size. The magnification must be of central (not lenticular) origin, since the monocular slide having the defect has been kept in sharp focus throughout. If the diplopia disappears at the same instant that the monocular slide defect is gotten into correct focus, the demonstration is incorrect, and the tube divergence must be increased slightly to increase the diplopia. A position can be found which will give a clearly obvious time lag between the correction of the accommodation and the correction of the diplopia, with the described abrupt change in size. The only change occurring at the instant of sudden magnification is a simultaneous sudden decrease in convergence.

My second, and more interesting, observation in this matter is related to a curious case which came to my attention; I regret that she can no longer be reached for better systematic study. The woman, in her early thirties, presented herself for refraction, with no complaints except the slight inadequacy of her glasses. Her refractive error was of no consequence, and a minor change restored satisfactory acuity. During the refraction an apparent right hyperphoria of 2 △ for distance was found, but for some reason no duction tests were performed at this visit. She was given instead a pair of temporary prism clip-ons to wear over her old glasses. She wore the prisms for two weeks and returned to report complete indifference to them; they had no effect whatever, either favorable or adverse. At this time the duction measurements were taken and a remarkable picture appeared. The ductions seemed almost unlimited in all directions. She would promptly overcome a 5 D. prism base down before either eye, describing diplopia only during the fraction of a second it required for her to overcome the prism. A 5 D. prism base up was accepted just as readily. Vertically placed prisms of 5 D. with bases opposite before the two eyes did not disturb her; she again described only a fleeting instant of diplopia. Ten diopters per eye (a total of 20 D.) if applied gradually was overcome.

She was intelligent and cooperative and presented herself for periodic examination a number of times, displaying a ready grasp of all questions and much insight. She had always considered her eyes normal and denied there being any personal or familial history of strabismus. The existence of her ocular novelty did not weigh on her in the least, and she returned only to enable me to observe this unusual performance further. Under slowly moving Risley rotary prisms I repeatedly watched the behavior of her eyes. The eyes would deviate independently toward the apexes of the prisms to a remarkable degree. By increasing the base-down prism before one eye, I could make the eye turn higher and higher at the same time that base-up prism was forcing the other eye down-

ward. The eyes could be readily observed over the edges of the Risley prisms, and the effect was disconcerting. The cover test performed repeatedly by several trained observers failed to reveal any abnormality under closest scrutiny except the trace of right hyperphoria. She gave every evidence of cosmetic and functional binocularity to several observers on routine examination. Under the higher prism stresses she would describe distortions of various types; for example, a square window would be converted to an oblique lozenge, but would never appear double. I was unable, in my perplexity, to record trustworthy figures for her ductions; she seemed to reach variable, but always extreme, end points in accordance with anatomic limitations and fatigue. The more vigorous applications of prism would cause fleeting dizziness, which she calmly ascribed to distortion of her field. She rejected the higher strengths of vertical prism clip-ons for interval wear between visits because of the distortion, but never because of diplopia. She accepted up to 6 D. with base up or base down on either eye for prolonged wear (days) with the intelligent description of only minor nuisance value. On removing the clip-ons, one could see the eyes in their abnormal positions for an instant before they assumed a common level; she described diplopia during these quick adjustments.

The horizontal ductions behaved similarly, both with Risley prisms and with the major amblyoscope. As base-out effect was increased, she described the usual minification and recession of her image, but would hold a single image to the maximum available with the instruments. The eyes would visibly be turned in very strongly and would elicit a description of a slight and transitory pulling sensation in the areas of the outer canthi; I presumed that these sensations originated from the check ligaments. A base-in effect caused the eyes to diverge; beyond 20 △, she seemed to lose control in some manner which she could never fully explain but which she firmly insisted was not doubling of her images. As the base-in effect was increased, she described magnification of her image, which seemed to draw closer. I believe her confusion at 20 △ base in was probably due to this magnification and approximation, with loss of the image within her near point; i. e., it was due to inability to diverge beyond 20 △ and accommodate for near point simultaneously! On the Keystone stereoscope, with the familiar stereopsis card, she was unable to demonstrate any third degree fusion on repeated trials. She readily demonstrated pseudostereopsis with coins, pencils, and the like, but her monocular behavior was as good as the binocular. A Verhoeff stereoptor* unfortunately, was not available.

In an effort to determine a basis for possible prism needs, I asked her to return some evening when she felt unusually fatigued; she did so and provided another most interesting exhibition. On the major amblyoscope, I first applied divergence; when she reached the area of 12 △, I thought I detected a tremor or flutter in her eyes. Repeating the maneuver several times very slowly and watching each lateral limbus with a hand loupe, I found a variable point in the 12 △ divergence area where she would display a very fine conjugate horizontal oscillation, too rapid to count, but probably of almost the flicker or frame frequency of early motion pictures. At this threshold she still denied diplopia but described a rather pronounced blurring of her image. Beyond this point she elected left fixation and described immediate diplopia as the right eye resumed cosmetic parallelism.

I have deeply regretted the haphazard nature of those examinations, for subsequent deliberation convinces me that this woman's ocular behavior holds

information of possible value. I believe that she maintained her almost perfect, and remarkably deceptive, cosmetic and functional binocularity by means of exceedingly rapid alternation—alternation in the psychic or integrative sense—and that visible (slowed down?) physical alternation occurred only under induced stress with the impediment of fatigue.

Her interesting exhibition may have the significance of a "missing link" in the fusion problem. As a rather crude demonstration of this mechanism, one may mentally picture two glass tubes 1 meter in length and a few centimeters in diameter standing erect, side by side. One may then picture a large cork in each tube, the cork being slightly smaller than the tube, so that it can drop through with perfect freedom and no friction and yet fit the tube reasonably well. One may then imagine a mechanical device in the bottom of each tube which will project or shoot small round metal shot upward against the bottom of each cork. By synchronization of the frequency and velocity of the upward streams of shot, it would be a simple matter to make the corks rise equally in the tubes. Firing the shot with greater force would send the corks higher; reducing the force of the shot would let the corks ride lower in their cylinders. If the shots were fired with sufficient frequency, the inertia of the corks would cause them to ride motionless in their tubes; reducing the number of shots per second below the inertia reaction time of the corks would impart a visible jiggling or flutter to the corks. This simple experiment is admittedly crude, with various mechanical flaws, but may serve to demonstrate the idea. I have therefore toyed with the hazardous thought that this patient may hold a clue to the nature of fusion; that fusion may indeed be based on a rapid neurologic alternation of two dissimilar images, with ocular parallelism enforced in most people by the speed of the alternation. This patient's lack of true stereopsis does not necessarily militate against this view if her condition is considered a borderline one, lying between the physiology of "normal" binocularity and that of manifest strabismus. As a corollary, one might again revive the theory that strabismus occurs in persons who have defective synchronization of the paired oculoneural "stroboscopes."

SUMMARY

Two observations on the voluntary dissociation of the accommodation and convergence faculties are discussed. The first observation suggests that the psychic concept of the location of the horopter in space is primarily related to convergence, rather than to accommodation. It also suggests that the psychic magnification of near objects and minification of distant objects in excess of that based on the law of the square

of the distance is predicated on convergence primarily, rather than on accommodation.

The second observation involves an unusual case of fusion anomaly in which lifelong functional parallelism appeared to depend on alternation at or above the frequency of flicker. It is believed that this case may be evidence in favor of the theory of physiologic alternation as a basis of fusion.

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A SURGICAL APPROACH TO THE INFERIOR OBLIQUE MUSCLE

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DR. JAMES WATSON WHITE was the first to operate on the inferior oblique muscle at its insertion, when, in 1936, he performed a recession of its tendon on the globe. He described the surgical technic, and the highly successful results obtained, in the June 1943 issue of the *American Journal of Ophthalmology*.[1] The procedure was immediately recognized as a most significant contribution to ophthalmic surgery, and repetition by others of Dr. White's faultless result attests its value.[2] It seems appropriate, therefore, to refer to this operation—the recession of the tendon of the inferior oblique muscle—as the James Watson White operation.

In doing the White operation at the New York Eye and Ear Infirmary, without detaching the lateral rectus muscle, I have not found the usual approach through the conjunctiva completely satisfactory. The incision is usually made downward from the tendon of the lateral rectus muscle, and at no place does it directly expose the inferior oblique muscle. A search of the literature did not reveal any suggestion for a better exposure. An approach which seems an improvement is therefore submitted. This method was developed in the clinic of Dr. Raymond Emory Meek.

Surgical approach to the inferior oblique muscle at its insertion, when the lateral rectus muscle is not detached, is not an easy task.[3] With the method I have seen used, the surgeon locates the muscle by making blind sweeps with a muscle hook. If and when the muscle is brought into the conjunctival wound, it is hidden by the bulbar fascia of Tenon. This fascia must be dissected to expose the muscle and its tendon. Each time the muscle slips off the hook, this procedure is repeated, resulting in mutilation of the bulbar fascia of Tenon. Good exposure and convenient working conditions are only occasionally

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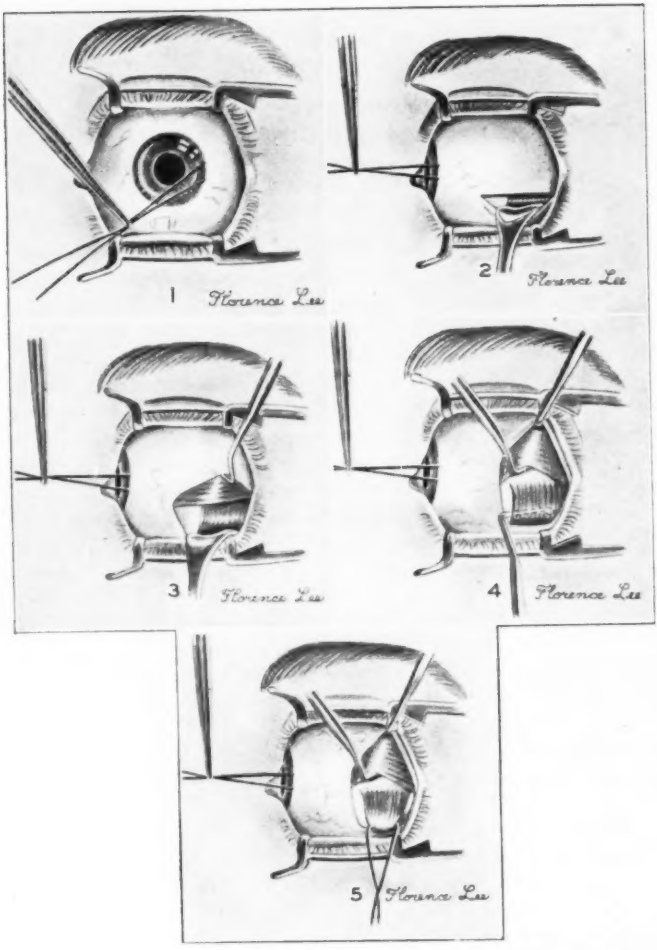
†Dr. Johnson died July 13, 1948.

Read before the New York Academy of Medicine, Section of Ophthalmology, Jan. 20, 1947.

1. White, J. W.: Surgery of the Inferior Oblique At or Near the Insertion, Am. J. Ophth. **26**:586 (June) 1943.

2. McDannald, C. E.: Unpublished data.

3. Berens, C., in discussion on White.



(1) A traction suture is placed in the temporal limbus. (2) The globe is held in the position of extreme adduction by traction on the suture; the drawing shows the position of the conjunctival incision and its relation to the inferior oblique muscle, which is exposed to view by the Desmarres retractor. (3) A muscle hook elevates the upper edge of the opening in the conjunctiva and Tenon's fascia in order to show the lateral rectus muscle overlying the global end of the inferior oblique muscle. (4) A muscle hook elevates the conjunctiva, with exposure of the lateral rectus muscle, which, in turn, is elevated by another hook, with exposure of the insertion of the inferior oblique muscle. (5) A suture replaces the muscle hook around the inferior oblique muscle.

During the actual surgical procedure, neither the upper edge of the conjunctival incision nor the lateral rectus muscle need be retracted.

obtained. As other troublesome accidents, the surgeon may (1) seize the inferior rectus muscle on the muscle hook by mistake, either alone or with the inferior oblique muscle; (2) sever the inferior rectus muscle from the globe, because he has mistaken it for the inferior oblique muscle; (3) injure the inferior rectus muscle necessitating later resection; (4) split the lateral rectus muscle by catching its lower half on the muscle hook, and (5) sever or damage the branch of the oculomotor nerve supplying the inferior oblique muscle.

These problems are all encountered as a consequence of the remoteness of the usual conjunctival incision from the muscle. When the incision does not overlie the inferior oblique muscle, direct exposure is impossible. Placement of the new incision and the technic of exposure to be described afford a direct view of at least a portion of the muscle, and the surgeon is thus enabled to pass the muscle hook more correctly and with greater ease.

OPERATIVE TECHNIC

The globe is held in the position of extreme adduction by traction exerted on a suture placed in the limbus on the lateral side of the cornea and held by an assistant. The suture used is 00 braided silk on an atraumatic needle. If the limbal suture is not used, adduction may be obtained by means of a muscle hook placed under the tendon of the lateral rectus muscle.

With a Lester forceps the conjunctiva is picked up just below the lower border of the lateral rectus muscle, at a point midway between the limbus and the outer canthus. The conjunctival incision is continued horizontally along the lower border of the lateral rectus muscle to the lateral fornix.

The bulbar fascia of Tenon will then be exposed in the conjunctival wound. At the outer canthus this fascia is cut and spread apart with a pair of Stevens scissors. The inferior oblique muscle will be seen through the opening in Tenon's fascia. The fascia is retracted with a Desmarres retractor. The extent of muscle thus exposed varies from its anterior border alone to over one-half its width. The amount of muscle exposed is directly proportional to the width of the palpebral fissure, the amount of backward bowing of the lateral orbital margin, the length of the lateral check ligaments and the length of the optic nerve. It varies inversely with the amount of the retrobulbar injection. The amount of muscle exposed also varies with the position of insertion of the muscle into the sclera—the closer to the cornea the insertion, the greater will be the exposure of the muscle.

A hook is next passed around the muscle. If any fascia is included, another hook should be placed so as to exclude Tenon's fascia from its grasp. A suture (from 0 to 000 in size) is next passed around the muscle. The ends of the suture are secured by a suture clip. Should the muscle slip off the hook, the suture enables the surgeon to replace the hook without further trauma to Tenon's fascia. Should the hook not be replaced, a recession operation may be completed without it.

With Lester forceps and a Stevens scissors, Tenon's fascia is dissected away from the muscle and its tendon. Under no condition should any dissection be made along the muscle more than 5 mm. beyond its insertion because of the danger

of injury to the nerve. This nerve enters the posterior border [4] or the upper border [5] of the muscle about 12 mm. from the globe. The inferior oblique muscle is now ready for operation.

COMMENT

The usual approach for exposure of the inferior oblique muscle has been discarded, for the reasons stated. With the method described, an incision is made parallel with the external rectus muscle and extended along its lower border to the lateral fornix; thus the inferior oblique muscle is more satisfactorily exposed and is more readily accessible.

118 East Sixty-Fifth Street.

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5. Wolff, E.: The Anatomy of the Eye and Orbit, ed. 2, Philadelphia, The Blakiston Company, 1940, p. 182.

STUDIES OF THE EYE WITH RADIOSODIUM AUTOGRAPHS

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ARTIFICIAL radioactive isotopes were introduced for turn-over studies on the eye by Kinsey, Grant, Cogan, Livingood and Curtis.[1] These investigators used Na^{24}, P^{32} and Cl^{38} in their work with rabbits. Recently, Wang[2] studied the movement of radioactive sodium and chloride in dogs, whereas Visscher and Carr[3] (in dogs) and Scholz, Wilde and Cowie[4] (in guinea pigs) limited their study to radiosodium. These investigations revealed the steady state ratios of the tracer elements between plasma and ocular fluids and the turnover rates of these constituents in the aqueous humor. The investigations of Visscher and Carr[3] and Wang[2] included studies on the rate of entrance of the radioactive elements into the cerebrospinal fluid. All these results confirmed the impression of the usefulness of radioactive elements as tracers in biologic studies. Quantitative data of great accuracy were secured by measuring (with the Geiger-Müller counter) radiations

Supported by the Knapp Memorial Foundation.

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Read in part at the Three Hundred and Eighty-First Meeting of the New England Ophthalmological Society, Boston, Feb. 18, 1948.

1. Kinsey, V. E.; Grant, W. M.; Cogan, D. C.; Livingood, J. J., and Curtis, B. R.: Sodium, Chloride and Phosphorus Movement and the Eye Determined by Radioactive Isotopes, Arch. Ophth. **27**:1126-1131 (June) 1942.

2. Wang, J. C.: Penetration of Radioactive Sodium and Chloride into Cerebrospinal Fluid and Aqueous Humor, J. Gen. Physiol. **31**:259-268 (Jan.) 1948.

3. Visscher, M. B., and Carr, C.: The Rate of Entrance of Radio Sodium into the Aqueous Humor and Cerebrospinal Fluid, Am. J. Physiol. **142**:27-31 (Aug.) 1944.

4. Scholz, R. O.; Cowie, D. B., and Wilde, W. S.: Studies on the Physiology of the Eye Using Tracer Substances: I. The Steady-State Ratio of Sodium Between the Plasma and Aqueous Humor in the Guinea Pig, Am. J. Ophth. **30**:1513-1515 (Dec.) 1947. Wilde, W. S.; Scholz, R. O., and Cowie, D. B.: Studies on the Physiology of the Eye Using Tracer Substances: II. The Turnover Rate of Sodium in the Aqueous Humor of the Guinea Pig: Methods of Analysis, ibid. **30**:1516-1523 (Dec.) 1947.

emitted by the radioactive elements in samples of ocular fluid after their introduction under various conditions.

Although the counter technic eliminates many errors and facilitates quantitative studies, it does not provide maximum information on the topographic relation of the tracer atoms within individual structures of the eye. Such a purpose seems better served by radioautography, which under certain conditions is suited to determination of actual location and differences of concentration of the radioactive elements with respect to histologic landmarks. The technic makes use of the photographic action of the radiations emitted by the tracer substances. Thus, the photographic plate gives a visible representation of the distribution of the labeled atoms in sections or slices which have been placed on the radiosensitive emulsion.

The method is not new, as the principles were recognized and used forty years ago by Mügge [5] to locate, topographically, radioactivity in minerals. About twenty years later, Lacassagne, Lattès and Lavedan [6] studied the deposition of a naturally occurring radioelement (polonium) in renal tissue of the rabbit. In the last ten years, after radioisotopes of elements which occur normally in tissues were made artificially, the method has been employed to investigate (histologically) the localization of radioactive iodine in the thyroid, phosphorus in lymph glands and strontium in bone. These radioactive isotopes have a relatively long half-life (as compared with the 14.8 hours of Na^{24}) and are deposited preferentially in the tissues in which radioautographs have been obtained. Hamilton, Soley and Eichorn [7] produced many excellent autographs of radioiodine in the thyroid by fastening the tissue section (temporarily) very close to the photographic plate. Permanent alinement of tissue and autograph was obtained by Belanger and Leblond,[8] in coating the tissue with emulsion removed from a photo-

5. Mügge, O.: Radioaktivität und pleochroitische Höfe, Zentralbl. f. Min., Geol. u. Paleont., 1909, pp. 65, 113 and 142.

6. Lacassagne, A., and Lattès, J.: Mise en évidence par l'autoradiographie des organes, des localisations histologiques du polonium injecté dans l'organisme, Bull. d'histol. appliq. à la physiol. **1**:279-283, 1924. Lacassagne, A.; Lattès, J., and Lavedan, J.: Étude expérimentale des effets biologiques du polonium introduit dans l'organisme, J. de radiol. et d'électrol. **9**:1-14, 1925.

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8. Leblond, C. P.: Locating Iodine in Tissues Autographically Especially After Fixation by Freezing and Drying, Stain Technol. **18**:159-164 (Oct.) 1943. Belanger, L. F., and Leblond, C. P.: A Method for Locating Radioactive Elements in Tissues by Covering Histological Sections with a Photographic Emulsion, Endocrinology **39**:8-13 (July) 1946. Leblond, C. P.; Percival, W. L., and Gross, J.: Autographic Localization of Radio-Iodine in Stained Sections of Thyroid Gland by Coating with Photographic Emulsion, Proc. Soc. Exper. Biol. & Med. **67**:74-76 (Jan.) 1948.

graphic plate, and by Evans,[9] in mounting the tissue section directly on the photographic emulsion of a plate or film. In these processes, the preparation was first developed photographically and then subjected to histologic staining procedures. The reduced silver grains of the emulsion were closely superimposed on histologic details and were well alined to the finer structures of the thin sections.

In the present study, a first attempt was made to use radiosodium for radioautographic studies of the tracer in the eye. In view of the relatively short half-life of this radioisotope and the fact that there is no preferential binding of sodium to structural and chemical constituents of the ocular tissues, the technic in the work with iodine and other isotopes had to be modified or replaced with new methods.

MATERIALS AND METHODS

Two principal methods of radioautography were selected. First, the technic developed by Evans [9a] for studies on the distribution of iodine in the thyroid gland was applied to thin tissue sections of eyes of experimental animals. Since a description of this procedure is not readily available to ophthalmologists, it will be presented here in brief form as it was used on the eye.

The tissue was fixed and dehydrated in acetone or absolute alcohol (three changes, three to five minutes in each change), embedded in paraffin and cut in sections 10 to 12 microns in thickness. Ribbons containing two or more sections each were spread on water at approximately 42 C. and then quickly transferred to a vessel with cool water. In the darkroom, films (kodak dental x-ray film ultraspeed®) or plates (kodak lantern slide medium contrast plate® 2 by 2 inches in size) were slipped under the floating sections to lift them from the water. The preparations, consisting of the sections on films or plates, were dried by a fan and stored in light-tight boxes. On the following day, the paraffin was removed in a xylene bath, and (after drying) the preparations were returned to the storage boxes for the desired time of exposure. The photographic films or plates with the tissue sections in place were developed in a developing solution (Eastman D-11,® for example) for two to five minutes and further processed in the usual way. The sections were then stained with Delafield's hematoxylin (overstained) and passed through acid water; the emulsion on the back of the film was removed by scraping, and the sections were then passed through ammonia water, stained with eosin, dehydrated, cleared and mounted in balsam. The tissue for the microscopic sections was obtained in three ways: (1) by removing the iris and ciliary body after opening the globe by an equatorial section; (2) by keeping intact the entire anterior segment without lens; (3) by cutting slices from frozen globes adjacent to the vertical meridian plane.

The second method used was one of gross examination and has not been described before. The experimental animal received the radioactive tracer material by local or systemic route and was killed after a planned interval by intravenous

9. Evans, T. C.: (*a*) Preparation of Radioautographs of Thyroid Tumors for Study at High Magnification, Radiology **49**:206-213 (Aug.) 1947; (*b*) Radioautographs in Which the Tissue Is Mounted Directly on the Photographic Plate, Proc. Soc. Exper. Biol. & Med. **64**:313-315 (March) 1947; (*c*) Selection of Radioautographic Technic for Problems in Biology, Nucleonics **2**:52-58 (March) 1948.

injection of an overdose of sodium pentobarbital. Death occurred after a few seconds, and the eyes were enucleated with as little trauma as possible. They were rinsed in isotonic sodium chloride solution U.S.P. and frozen by being embedded in solid carbon dioxide U.S.P. for five minutes and in a freezing mixture of dry ice® and alcohol for an additional five minutes. The frozen globes were bisected meridionally with chilled razor blades and microtome knives. By cutting a broad calotte from each half, two slices were obtained which measured in thickness between 1.5 and 2.5 mm., and their surfaces were made smooth by paring. The slices were cut by hand as evenly as possible. Care was taken to maintain the tissue in the frozen state during the preparation of the slices. For photographic exposure, each preparation was placed in an individual paraffin-lined container, which held the slice in close apposition with the sensitive film (kodak dental x-ray film ultraspeed®). The latter was protected by a single layer of cellophane. Here, again, precaution was taken to prevent any, even superficial, melting of the frozen slices. For this purpose, the containers were kept for the period of film exposure in a "deep freeze" chest. When radiosodium had been given by systemic injection, the films were exposed for forty-eight hours. After local administration of the tracer material, the time of exposure was adjusted to the expected amount of radiation from Na^{24} in the preparation. The procedures of developing, fixing, washing and drying were the same as those applied in the preparation of thin paraffin sections. In most instances the slices were photographed to permit comparison of anatomic details with the radioautograph.

The radioactive sodium was produced in the cyclotron at Columbia University (department of physics) and arrived at the laboratory as a very dilute (approximately 0.01 per cent) solution of sodium chloride. The radioisotope represented only a small part of the total sodium content. A volume of the solution, containing the desired amount of radioactivity, was evaporated to dryness and later redissolved to a final concentration approximately that of isotonic solution of sodium chloride.

Preliminary experiments were carried out on the photographic effect of agar disks containing a measured amount of Na^{24}. Disks 11 mm. in diameter and 1.5 or 3 mm. in thickness, containing 0.1 microcurie, produced a moderate darkening of the (dental x-ray) film, which had been exposed for forty-eight hours and developed in Kodak Developer D-11 for two minutes. A disk of plain agar (1.5 mm. thick) between the film surface and the radioactive disk almost completely prevented the photographic effect under similar conditions of exposure. This was also the case when the amount of the Na^{24} in the superimposed disk was tripled and the thickness of the interposed layer of nonradioactive agar was changed to 2.5 mm. The placing of a layer of cellophane between the radioactive material and the photographic emulsion did not appreciably influence the intensity and sharpness of the autograph. It is planned to report, in a later paper, the quantitative values of film darkening by agar disks of different degrees of radioactivity under standard conditions.

ENTRANCE OF RADIOSODIUM INTO OCULAR FLUIDS FROM THE BLOOD

Technic.—Intraperitoneal injection of a solution containing radiosodium was selected as a general route. The technic of Kinsey, Grant, Cogan, Livingood and Curtis [1] was followed in that radioactive sodium was dissolved in 5 cc. of isotonic sodium chloride solution. The amount of the artificial radioactive element injected, expressed in terms of radioactivity, varied between 0.6 and 0.8 millicurie per kilogram of body weight. The intervals between injection and enucleation were 30 minutes, 1 hour, 2 hours and 4 hours, respectively. The study was carried out on 8 chinchilla rabbits, which averaged 2.5 Kg. in weight. Two cats,

a dog and a monkey were given similar injections to determine whether any species difference could be noted. In this series of experiments the gross method of autoradiography with frozen slices was used. When the paraffin section technic was tried, the relatively small amount of radiosodium in the preparations was apparently lost prior to embedding, so that no photographic effect was produced.

Results—At the earliest interval, of thirty minutes, the radioactive material appeared in the rabbit's eyes predominantly in the region of the ciliary body, choroid and optic nerve, as interpreted by the maxima of darkening of the film emulsion. From the region of the

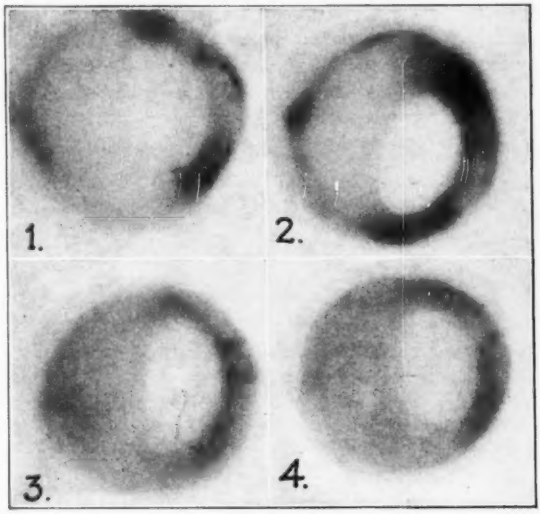

Fig. 1.—Radioautographs of rabbit eyes (*1*) thirty minutes, (*2*) one hour, (*3*) two hours and (*4*) four hours after intraperitoneal injection of radioactive sodium, 0.6 to 0.8 millicurie per kilogram of body weight.

ciliary body the tracer element permeated the vitreous at its base. Another, less marked, accumulation of radioactive sodium was indicated on the film at the posterior part of the vitreous, in front of the optic nerve. These two localities represented the main portal of entry of the labeled ions into the vitreous, whereas the spreading of radioactive sodium from the choroid through the retina was of a lower degree (fig. 1).

So far as the anterior segment of the eye was concerned, autoradiographs of the early stages suggested that in the rabbit eye the tagged sodium diffused after passing through the walls of the ciliary

capillaries into the extracellular fluid of the processes and of the iris, entering chiefly by this route the aqueous in the anterior chamber. The degree to which the capillaries of the iris participated in the passage of labeled sodium from blood to aqueous humor could not be determined. In the few experiments on the dog (2 eyes), the cat (4 eyes) and the monkey (2 eyes), the observations were made one hour after injection of radiosodium, an interval comparable to that for the rabbit; however, the darkening of the area of the ciliary body in films from the dog and the monkey was not so intense as in films from the rabbit. In the experiments on the cat there was no difference between the darkening of the region of the ciliary body and that of the neighboring areas. In these species, as in rabbits, radioactive sodium entered the vitreous predominantly at its base and in the area Martegiani (fig. 2).

A second possible mechanism, that is, active transfer of the tracer across the barrier of the ciliary epithelium into the posterior chamber,

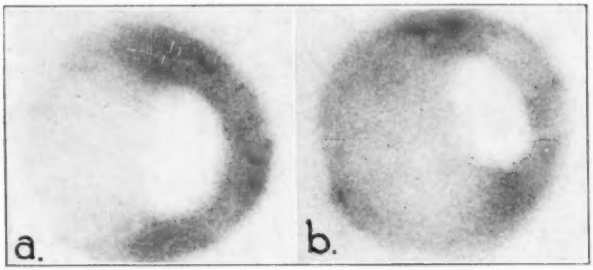

Fig. 2.—Radioautographs of (*a*) cat eye and (*b*) dog eye one hour after intraperitoneal injection of radiosodium, 0.6 to 0.8 millicurie per kilogram of body weight.

followed by diffusion through the pupil into the anterior chamber, must be considered in the later stages. An attempt was made to procure visible evidence of such a secretory mechanism in the transport of radioactive sodium from blood to the fluids of the eye. The simplest way to distinguish between active transfer or secretion and passive penetration seems to be to cut off by the use of metabolic poisons the source of energy by which this transfer operates. For this purpose, a 0.5 per cent solution of sodium cyanide was introduced into the anterior segment of the eye by iontophoresis from the negative pole (2 milliamperes for five minutes). On the basis of previous investigations[10] on the inactivation of the cytochrome oxidase in the ciliary

10. von Sallmann, L.: Controversial Points in Ocular Penicillin Therapy, Tr. Am. Ophth. Soc. **45**:570-636, 1947.

epithelium with this technic, the metabolic inhibitor was administered twenty minutes prior to the intraperitoneal injection of radioactive sodium, and the experiments were terminated after one or two hours. Introduction of cyanide into the anterior part of the eye resulted in a notable increase in the protein permeability of capillaries of the ciliary region. Therefore, in the control eyes, a similar effect on these capillaries was produced with histamine iontophoresis, which has been shown not to interfere with the action of the cytochrome oxidase. Histamine dihydrochloride (0.1 per cent) was used, the electric field being applied with the anode on the eye for two and one-half minutes at 1 milliampere. The experiment was repeated five times.

Although the radioautographs of both eyes showed similarity in the general distribution of the radioactive sodium, a somewhat circumscribed and much denser darkening of the film was observed

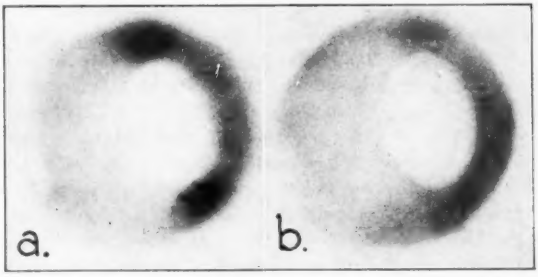

Fig. 3.—Radioautographs of rabbit eyes one hour after intraperitoneal injection of radiosodium: (*a*) eye pretreated with cyanide and (*b*) eye pretreated with histamine by iontophoresis.

in the area corresponding to the ciliary body in the slices of eyes treated with the metabolic poison (fig. 3). Hence, there was suggestive evidence in the radioautographs that the inhibition of the secretory mechanism by cyanide resulted in accumulation of the tracer element in the region of the ciliary body.

Comment.—In previous experiments [11] with the dye T-1824 on eyes with increased permeability of the capillaries, the movement of the dye-albumin complex was followed. It was concluded that in the early phase, after intravenous injection of the dye, the colored material passed through the walls of the ciliary capillaries into the tissue interstices of the ciliary processes, and from there into the iris and the aqueous

11. von Sallmann, L., and Dillon, B.: The Effect of Diisopropyl Fluorophosphate on the Capillaries of the Anterior Segment of the Eye in Rabbits, Am. J. Ophth. **30**:1244-1262 (Oct.) 1947.

humor of the anterior chamber. The capillaries of the iris also were dilated, but obviously did not permit passage of the blue material. It is unlikely that the gradient of permeability between the capillaries of the iris and those of the ciliary body as observed for colloids could exist for crystalloids, since it is thought that the capillary walls throughout the body allow simple physical diffusion of these substances. It can be assumed, therefore, that the capillaries of the ciliary body, as well as the capillaries of the iris, permit the movement of radiosodium from the blood to the fluids of the eye.

Kinsey and Grant [12] calculated by mathematical formulation and integration of their experimental results that radioactive sodium and other monovalent cations enter the anterior chamber as a result of a secretory process; that is, their experimental findings were incompatible with the hypothesis of pure ultrafiltration or dialysis. The difference between the radioautographs of cyanide-treated eyes and those of histamine-treated eyes suggested that the process of active transfer was operative in the entry of radiosodium from blood to aqueous humor across the barrier membranes of the ciliary body, thus lending support to the concept of Kinsey and Grant. However, alternative explanations must be considered. It is possible that cyanide increased the permeability of ciliary capillaries more than did histamine, although the protein content of the aqueous humor was similarly raised by the iontophoretic introduction of each of these substances. On the other hand, the absence of a pronounced radioautographic effect at the region of the ciliary body in the histamine-treated eyes may have been induced by a more pronounced action of the drug on the capillaries of the iris.

DIFFUSION OF RADIOSODIUM IN THE EYE AFTER INTRAVITREAL INJECTION

Technic.—Radioactive sodium was introduced directly into the vitreous (1) to compare the diffusion of the tracer element in the vitreous of the living eye and in the enucleated globe, and (2) to reinvestigate the problem of resorption of electrolytes from the vitreous by the columnar epithelium of the pars plana of the ciliary body.

The radioactive sodium was injected into the vitreous of rabbits with a 30 gage needle in 0.025 to 0.06 cc. of fluid with the eye under local anesthesia. The amount of radiosodium, expressed in terms of radioactivity, ranged from 10 to 60 microcuries, with the higher dose occasionally administered. A needle 1 cm. in length was inserted beneath the superior rectus muscle about 6 mm. behind the limbus. It was directed toward the posterior pole of the eye. The eyes were removed at intervals of 1, 2, 3, 4, 6, 8, 10, 12, 18 and 24 hours. After enucleation, the eyes were frozen, sliced and used for radioautographs, as described in the first part of the paper. Film exposure times varied in accordance with the amount of

12. Kinsey, V. E., and Grant, W. M.: The Mechanism of Aqueous Humor Formation Inferred from Chemical Studies on Blood-Aqueous Humor Dynamics, J. Gen. Physiol. **26**:131-149 (Nov.) 1942.

radioactive material injected. Fifty eyes were examined in this series. In the group in which diffusion was studied in the enucleated globes, the injection was made immediately after excision, and the globes were suspended in individual moist chambers, kept at 37 C. They were removed in series, at 1, 2, 4 and 6 hours, to be frozen, sliced and used for radioautographs. The control eyes given injections intra vitam were enucleated at the time intervals previously indicated and processed in the usual way. As a rule, from each eye two frozen slices next the meridional plane were available for the radioautographs.

Results.—Under the conditions of the experiment, diffusion of the labeled ion in the living eyes was rapid, and, as expected, occurred at a much faster rate than had been observed with penicillin or hemoglobin, studied previously. The radioactive element had apparently diffused through more than two thirds of the vitreous within one hour, but was still unequally distributed after two hours, whereas after four hours the intensity of the darkening of the film was homogeneous in the region corresponding to the vitreous space. With this method, traces of radiosodium could be demonstrated in the aqueous humor one hour after the intravitreal injection. The distribution of the electrolyte in the anterior and in the posterior segment of the eye approached equality at a ten hour interval; later, that is, twelve, eighteen and twenty-four hours after injection, the content of the anterior chamber emitted a moderate amount of radiation, in contrast to the vitreous space, in which the photographic effect of the tracer was still very marked. The region of the ciliary body, and also of the optic nerve, stood out in a few radioautographs as darker areas, suggesting a preferential route of absorption. This observation will be considered later in the experiments on absorption from the vitreous.

In removed globes the radiosodium seemed to diffuse at a lower rate. No relative decrease of darkening of the film in the region corresponding to the anterior chamber was seen at the later intervals when the film was compared with the photographic effect in the area representing the vitreous space. There was no contrasting darkening of the region of the ciliary body, such as was observed in the living eyes.

Comment.—It was shown in the experiments with agar disks containing low concentrations of Na^{24} that the labeled ion at a distance greater than 1.5 mm. from the film reduced the silver granules to a negligible degree. Therefore, radioautographs of thicker slices of the eye indicated principally the distribution of the radiating atoms within the layers nearest the film surface. This condition, the standardization of the intravitreal injection and of the slicing of the globes and the comparison of the pictures obtained from the two slices in each instance, permitted evaluation of the speed of diffusion of the radiosodium within the cavities of the eye. However, intravitreal injection of any material, even in minimal quantities or with a minimum of trauma,

necessarily disturbs physiologic equilibriums. It was for this reason that the data on the living and on the removed eye had significance only in a relative sense. The faster disappearance of sodium from the anterior chamber of the living eyes than from that of the enucleated globes, in contrast to the behavior of the tracer in the vitreous space, favors the theory of a through and through circulation of the tracer. A net loss of sodium by molecular exchange between the fluids and the circulating blood could hardly explain the differences in the radioautographs of the later stages in the two sets of experiments.

REABSORPTION OF RADIOSODIUM FROM THE VITREOUS

Studies on reabsorption by the ciliary body have been variously reported in the old and the recent literature. Meller,[13] many years ago, described an occasionally intensive phagocytic and cytolytic activity of the epithelium of the pars plana on red cells in the vitreous. Recently, he found morphologic signs and color reactions in sections of human eyes which convinced him that the columnar epithelium at the base of the vitreous plays an important part in reabsorption of fluid and electrolytes from the posterior part of the eye. Meller [14] and his pupil Lekhraj [15] saw in the histopathologic signs an expression of a physiologic function of this epithelium. Ma and Pillat [16] expressed agreement with Meller's opinion, when they reported that india ink, soluble iron salts, cod liver oil and blood could be demonstrated within the ciliary epithelium two hours after injection of the substances into the vitreous of albino rabbits. No emphasis was placed on the epithelium of the pars plana in bringing about this accumulation of the test substances. On the basis of these observations and those of Friedenwald and Stiehler [17] on the permeability of the ciliary epithelium for certain dyestuffs, experiments with radioactive sodium were conducted in the present series on rabbits, although the pars plana of the ciliary body is not well developed in this experimental animal.

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13. Meller, J.: The Significance of the Ciliary Epithelium in the Absorption of Vitreous Hemorrhages, Arch. Ophth. **57**:134-146 (March) 1928; Ueber die Tätigkeit des Ziliarkörperepithels bei der Aufsaugung von Glaskörperblutungen, Ztschr. f. Augenh. **69**:113-117 (Sept.) 1929.

14. Meller, J.: Die Quellung der Ziliarepithelien als Ausdruck ihrer resorptiven Tätigkeit bei Behinderung des Abflusses, Arch. f. Ophth. **143**:360-388, 1941.

15. Lekhraj, A.: Ueber die aufsaugungende Tätigkeit der Zeller der Ziliarepithels, Arch. f. Ophth. **143**:322-331, 1941.

16. Ma, W. C., and Pillat, A.: A Study of the Function of the Columnar Epithelium of the Ciliary Body of Albino Rabbits, Chinese J. Physiol. **3**:363-370 (Oct.) 1929.

17. Friedenwald, J. S., and Stiehler, R. D.: Circulation of the Aqueous: VII. A Mechanism of Secretion of the Intraocular Fluid, Arch. Ophth. **20**:761-786 (Nov.) 1938.

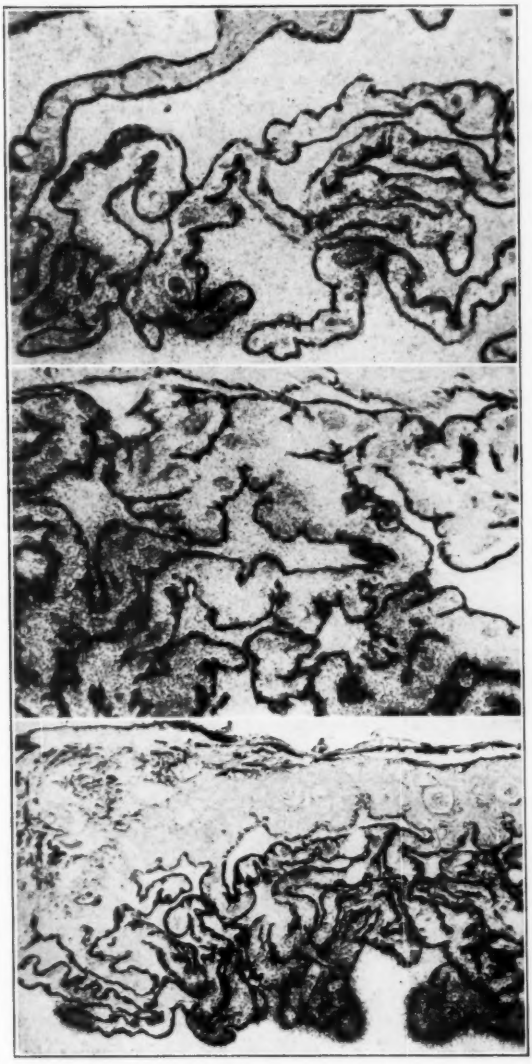

Fig. 4.—Radioautographs of sections of the ciliary body from rabbit eyes two hours after intravitreal injection of radiosodium, 100 to 300 microcuries.

Technic.—The technic of intravitreal injection was the same as that in the diffusion experiments, but the dose of the radiosodium introduced was increased to a range of 50 to 300 microcuries. Both the microscopic method of Evans, with thin paraffin sections, and the thick slice technic were employed. The globes were removed after 1, 2, 3 and 6 hours. Sections were placed on films for forty-eight hours or longer and slices for two hours or less.

Results.—The radioautographed sections showed occasionally a conspicuous accumulation of reduced silver grains in and around the ciliary processes, whereas the iris and retina did not contain more than a small number of background granules (fig. 4). With 1 exception, there was no indication that the epithelium of the pars plana was involved in the passage of the tracer into the tissue of the ciliary processes. In this 1 instance a moderate accumulation of reduced silver granules was noted in the loose tissue underlying the columnar epithelium of the pars plana. In a few radioautographs from thick slices the film presented considerably more intense darkening of the area which corresponded to the region of the ciliary body than of the anterior half of the vitreous space (fig. 5). This distribution was

Fig. 5.—Radioautograph of the anterior segment of the rabbit eye four hours after intravitreal injection of radiosodium, 40 microcuries.

not observed when the tracer material had been injected into the vitreous of enucleated eyes.

Comment.—Great precaution must be observed in interpreting these results. In the technic with thin paraffin sections the passing of the tissue through two or three changes of acetone or absolute alcohol and xylene washes out most of the sodium, and the subsequent complicated steps of the procedure in the darkroom may account for further loss of the tagged ions. This could explain why in many instances no radiation was demonstrated in any of the sections of a preparation. It is possible, therefore, that in the preparations with the photographically demonstrated accumulation of the tracer within the ciliary processes the radioactive substance had not entered these structures preferentially but, for unknown reasons, was not washed out from the ciliary processes to the same degree as from the iris or parts of the posterior segment of the eye. Since almost all radiosodium was removed during dehydration from the vitreous space, it could not be decided from the sections whether the accumulation of Na^{24} in the ciliary processes exceeded that at the base of the vitreous, that is, whether there was an indication

of movement against a concentration gradient or of the presence of a special driving force. Nevertheless, a few positive results observed with the thick slice technic on living eyes, in contrast to removed globes, suggests such a mechanism.

It was pointed out in the previous paragraph that the trauma of the injection places evaluation of such experiments on uncertain grounds. Furthermore, a biologic radiation effect must be considered possible in view of the relatively high dose of the radioactive element which had been introduced into the vitreous. For this reason, it seems premature to draw final conclusions from the observed phenomena and to bring them in line with Friedenwald's concept of ion transport by a mechanism of oxidation reduction. Kinsey and Grant showed that an apparent active secretion of ions of positive and negative charges may take place as a result of electric attraction of the secreted ions of positive charge for those of opposite charge, to maintain electrical equilibrium. A similar explanation could be adopted for a transfer from within out if Friedenwald's theory of ion transfer by secretion is accepted. An alternative explanation could be based on the hypothesis of Meller and co-workers that the columnar epithelium of the pars plana differs not only morphologically but functionally from the epithelium of the ciliary processes. No direct support for this theory was provided by the radioautographs or by the experiments of Friedenwald in which the selective permeability of the ciliary membranes for acidic and basic dyestuffs was described.

IONTOPHORETIC TRANSPORT OF RADIOSODIUM

In the last part of the study, radiosodium was used as a means to demonstrate movement of the substance in the eye under the influence of an impressed electric potential. The experiments were designed to follow the distribution of the tracer without inconvenient sampling errors, which are unavoidable in quantitative determinations of any substances in the vitreous humor.

Technic.—The electric field was applied in the form of (1) corneal iontophoresis, with the anode or the cathode on the eye; (2) iontophoresis of the ciliary body, in which the annular zone between the limbus and the ora serrata was used as the portal of entry for the galvanic current (a special applicator tube was made for this purpose); (3) corneal iontophoresis with an isotonic solution of sodium chloride used as electrolyte after the retrobulbar injection of 0.5 cc. of a solution containing radiosodium. Such a technic was described by Leopold[18] as useful in obtaining effective levels of streptomycin in the vitreous.

As a rule, a current of 2 milliamperes was applied for five minutes, and the eyes were removed for radioautography two to four hours after treatment. For

18. Leopold, I. H.; Wiley, M., and Dennis, R.: Vitreous Infections and Streptomycin: Experimental Studies, Am. J. Ophth. **30**:1345-1352 (Nov.) 1947.

all experiments a quantitity of sodium chloride which contained the radiosodium was dissolved in distilled water to furnish an activity of 100 microcuries per cubic centimeter of solution. Twenty rabbit eyes were used in this series.

Results (fig. 6).—Corneal iontophoresis with the anode on the eye resulted in a high concentration of the labeled ion in the anterior

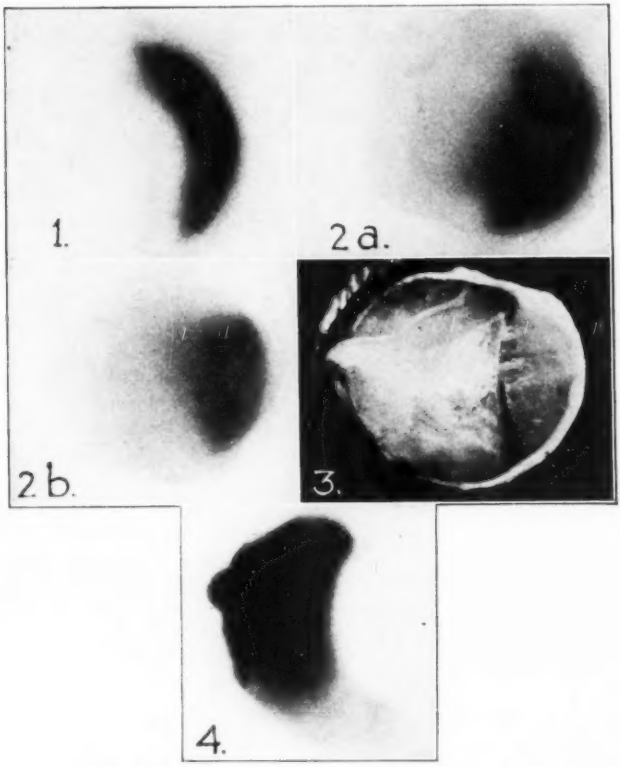

Fig. 6.—Radioautographs (*1*) of the normal rabbit eye two hours after corneal iontophoresis with radiosoduim, (*2*) of aphakic rabbit eyes (*a*) two hours and (*b*) four hours after corneal iontophoresis with radiosodium; (*3*) aphakic rabbit eye; (*4*) Radioautograph of normal rabbit eye two hours after iontophoresis of ciliary body with radiosodium.

chamber. This accumulation of the tracer was limited almost exclusively to this part of the normal rabbit eye. When the terminals were reversed and the cathode was used as the active electrode, scarcely any penetration was noticed on the film. It is evident with anode as the

electrode that true ion transfer took place and that diffusion of the undissociated salt through damaged epithelium played a minor part.

In aphakic eyes of rabbits, radiosodium was shown to diffuse from the anterior chamber into the vitreous when it had been introduced by corneal iontophoresis with the anode as the active electrode. The darkened area of the film occupied two hours after treatment a roughly triangular space in the middle third of the vitreous. If the interval between the application and the removal of the eye was prolonged to four hours, a moderate darkening of the film was equally distributed throughout the vitreous space. Total retinal detachment, which was present in the preparations of one aphakic eye, caused only a faintly discernible difference in the darkening of the film between the area corresponding to the vitreous body and that corresponding to the retroretinal space.

In general iontophoresis of the ciliary body did not produce easily demonstrable quantities of radiosodium in the vitreous space. Several times a faint darkening of the film was noted in a narrow zone of the peripheral region of this space. Exceptionally, radioautographs showed an intense darkening of the film in the area of the vitreous body of normal rabbit eyes with the lens in place. This darkening increased toward the posterior pole and the optic nerve. In the majority of experiments the radioactive element seemed to be accumulated in the anterior chamber, similar to the results accomplished with corneal iontophoresis. Changes in the design of the applicator tube, modification in the technic and the preceding use of vasoconstrictors have failed so far to reveal the cause of the irregularities of the results and to render the method reliable in producing appreciable sodium levels in the vitreous space.

Application of the electric field according to the method of Leopold in order to increase penetration of the tracer from Tenon's space into the posterior part of the eye was ineffective under the conditions of the experiment. A simultaneous use of vasoconstrictors did not influence the results.

Comment.—It was known from the work on penetration of antibiotics that corneal iontophoresis provided high concentrations of these test substances in the anterior segment of the eye. Radioautographs obtained with the use of Na^{24} confirmed these observations and demonstrated that the accumulation of the diffusible ion was practically confined to the area of the anterior chamber. The nature of the penetration as being essentially a true ion transport was indicated in the negative results when the pole on the eye was reversed.

The permeation of radiosodium from the anterior chamber into the vitreous in aphakic rabbit eyes could be well followed in the radioautographs. These observations emphasize the feasibility of introducing

antibiotics by corneal iontophoresis in infections of the posterior part of aphakic eyes.

Judged from the radioautographs, no iontophoretic method was found which provided a reasonably consistent level of the radioactive isotope in the vitreous of rabbit eyes with the lens in place. Iontophoresis of the ciliary body gave erratic results, and with the technic used the properly applied electric field after retrobulbar injection of the tracer material was disappointing.

SUMMARY AND CONCLUSIONS

1. Radioautographic technics were applied to studies of the movement of Na^{24} in the eye, a gross method being used for frozen slices and the microscopic method of Evans for thin paraffin sections of the eye.

2. Phases in the penetration of the tracer substance from the blood into the fluids of the eye were made visible. The regions of the ciliary body and of the optic nerve were shown as the main portals of entry. Diffusion through the capillary walls was found to be the predominant factor in this process.

3. Cyanide as a specific inhibitor of energy-providing reactions was employed to determine the existence of a second factor operative in the transport of Na^{24} from blood to the eye, that is, of active transfer by the barrier membranes of the ciliary processes. There was suggestive evidence that such a mechanism operates in the movement of sodium across the barrier membranes of the ciliary body.

4. Diffusion of Na^{24} in the vitreous and into the anterior chamber occurred at a rapid rate after intravitreal injection of the tracer. Its movement in the living eye exceeded that in the enucleated globe. Comparison of the radioautographs in the two sets of experiments supports the theory of through and through circulation of the tracer ion in the living eye.

5. The problem of absorption of electrolytes by the ciliary body was studied with Na^{24}, both methods of radioautography being used. A conspicuous accumulation of the tracer was observed in the ciliary processes after intravitreal injection, but no final conclusions could be drawn with regard to the nature of this phenomenon.

6. The influence of an applied electric field on the movement of Na^{24} in the eye was made visible by radioautography. Various types of iontophoresis were studied. None of them was suitable for the introduction of regularly substantial quantities of the tracer into the vitreous space, even though such technics did demonstrate appreciable penetration into the anterior chamber of normal eyes and into the vitreous space of aphakic eyes.

630 West One Hundred and Sixty-Eighth Street.

TREATMENT OF PEDICULOSIS CILIARIS WITH ANTICHOLINESTERASE AGENTS

Report of a Case

DAVID G. COGAN, M.D.
AND
W. MORTON GRANT, M.D.
BOSTON

NEW DRUGS for the treatment of pediculosis ciliaris cannot be said to be especially needed. The time-honored ammoniated mercury has proved itself effective when used liberally enough. Yet it is of considerable interest, and may be of some practical usefulness, to know that the common physostigmine in the standard concentrations used for the treatment of glaucoma is just as effective as ammoniated mercury, if not more so. Tetraethylpyrophosphate, and presumably many other anticholinesterase compounds, are also effective.

A case in which we had an opportunity to study the effect of physostigmine and tetraethylpyrophosphate is reported.

REPORT OF CASE

E. B., a woman aged 49, during routine refraction, was noted to have blepharitis. In reply to questioning, she stated she had had severe itching of the lids, especially at night. Gross examination showed black discoloration of the eyelashes and loose, tiny black dots on the cheeks below the lashes. The first impression was that of eyelash dye caked on the lashes. Examination with the slit lamp, however, showed that the discoloration was due to 100 to 200 nits adherent to the ciliary shafts of each upper lid and 20 to 40 nits on the shafts of each lower lid. Usually there were several of these nits to each hair shaft. The nit consisted of a chitinous case shaped like a cornucopia, with the large orifice facing outward. Approximately one tenth of the cases were empty. Less obvious were 5 to 7 adult pediculi on each upper lid and 1 to 3 pediculi on each lower lid. These parasites were partly embedded, head foremost, in the skin of the margin of the lid, with the posterior, clawlike legs in contact with the base of the cilia. The legs showed spontaneous movements most of the time. Characteristic were eight to ten brown dots arranged symmetrically on the back of each pediculus. The pediculi were transparent but contained pulsatile viscera with a reddish black content, which was presumed to be ingested blood. These contents were intermittently excreted, and the excreta comprised the black dots seen grossly on the patient's cheeks.

Nits were also found in the pubic area and the axillas, but none on the scalp. There was no preauricular or cervical lymphadenopathy.

To determine what effect anticholinesterase agents would have on the pediculi, tetraethylpyrophosphate and physostigmine were selected, since the dose of

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

these drugs tolerated by the eye was known. Accordingly, 1 drop of 0.01 per cent tetraethylpyrophosphate in purified kerosene was instilled onto the lids of one eye and 1 drop of purified kerosene without the drug onto the lids of the other eye. Within ten minutes the pediculi on the side on which the tetraethylpyrophosphate was used showed complete cessation of all visceral and limb movements, while the pediculi on the side where kerosene alone was used showed the usual visceral movements and a somewhat increased movement of the limbs. The following day the pediculi which had been exposed to tetraethylpyrophosphate were represented only by flattened carcasses, obviously dead, while those exposed to the control kerosene were normal. The nits appeared unchanged on both sides.

One drop of 0.01 per cent physostigmine base in kerosene was then applied to the lid containing the motile pediculi. No effect was evident on the pediculi, and a drop of 0.1 per cent physostigmine base in peanut oil was then instilled onto the lashes. The only effect observed over a thirty minute period was increased twitching of the limbs. Without further treatment, the patient was reexamined two days later and was found to have one small, presumably young, motile pediculus on each upper lid.

The impression was obtained, therefore, that 1 drop of 0.01 per cent tetraethylpyrophosphate had promptly killed the adult pediculi and that 1 drop of 0.1 per cent physostigmine base killed the adult forms more slowly, but that neither drug had prevented hatching of new pediculi from the nits.

To compare the effect of treatment with physostigmine with that of the usual ammoniated mercury, one eye was treated on two days with single instillations of 2 per cent ammoniated mercury ointment U. S. P. and the other eye with an ointment containing 0.25 per cent physostigmine base in petrolatum. Two days after the last instillation the patient was reexamined. The eye treated with physostigmine showed no adult pediculi, and there appeared to be a greater proportion of evacuated egg cases. The eye treated with ammoniated mercury showed 4 to 5 motile pediculi and no evident change in the nits.

The patient continued the treatment with ammoniated mercury in one eye and with physostigmine in the other. One week later there were no pediculi on either eye; and the nits, although no less in number, appeared somewhat shriveled up, and there was a greater proportion of empty cases. At this stage the pubic and axillary regions were treated by local application of Wyeth's bornate* (5 per cent isobornyl thiocyanoacetate and 0.6 per cent of dioctyle sodium sulfosuccinate). No further treatment was given the eyes.

The patient was reexamined two weeks and four weeks, respectively, after discontinuing treatment. The nits decreased in number spontaneously, and at the last visit the few remaining egg cases were all empty.

The patient's daughter, who, incidentally, slept with the patient, was examined on two occasions. At the first examination no pediculi or nits were seen. At a later examination a single pediculus and a single nit were found. These disappeared with the instillation of physostigmine ointment.

SUMMARY

The anticholinesterase drugs, tetraethylpyrophosphate (0.01 per cent in purified kerosene) and physostigmine ointment (0.25 per cent physostigmine base in petrolatum) were effective in the treatment of pediculosis ciliaris.

243 Charles Street.

INTRAVITREAL USE OF STREPTOMYCIN

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ALLENTOWN, PA.

EXPERIMENTAL studies concerning the use of streptomycin in treatment of intraocular infections have been published.[1] Since, as has been shown by Leopold and Nichols,[1a] streptomycin penetrates poorly from the blood stream into the normal vitreous humor, systemic administration of the drug is inadequate in therapy of infections of the vitreous. In a more recent series of experiments,[1b] Leopold demonstrated that streptomycin given by direct intravitreal, retrobulbar injection plus iontophoresis, or by irrigations of the anterior chamber reduced the severity of experimental infections of the vitreous due to Escherichia coli. These methods were effective in the order noted. The report further indicated that direct intravitreal injections of streptomycin produced retinochoroidal exudation and subsequent degeneration, but that in concentrations below 800 micrograms per injection the damage was minimal and was limited to the site of injection. Studies of retention of streptomycin in the vitreous [1c] indicated that after a single intraocular injection of 100 micrograms of the drug an adequate therapeutic concentration may be expected for over twenty-four hours.

That such experimental studies are of great clinical value is demonstrated by the following case, which is of particular interest because of the severity of the infection and the apparent sight-saving response to direct intravitreal injection of streptomycin.

REPORT OF A CASE

B. S., a Negro aged 26, was admitted to the Allentown General Hospital July 14, 1947, after injury from an accidental dynamite explosion while he was drilling a hole in rock preparatory to blasting.

Examination revealed that vision was clear in the right eye (i. e., when examined in the accident ward, the patient said he could see normally; no tests with Snellen notation were attempted) and was limited to light perception in the left eye. Both lids were swollen and showed numerous areas of penetration of rock dirt. The right eye showed a perforating wound of the cornea with a prolapse of the iris at 5 o'clock near the limbus. The lens and the visible portion of the fundus were clear.

1. (*a*) Leopold, I. H., and Nichols, A.: Intraocular Penetration of Streptomycin Following Systemic and Local Administration, Arch. Ophth. **35**:33 (Jan.) 1946. (*b*) Leopold, I. H.; Wiley, M., and Dennis, R.: Vitreous Infections and Streptomycin, Am. J. Ophth. **30**:1345, 1947. (*c*) Bellows, J. G., and Farmer, C. J.: Streptomycin in Ophthalmology, ibid. **30**:1215, 1947.

The left eye presented a perforating, 2 mm. laceration of the sclera at 4 o'clock about 3 mm. from the limbus. The cornea showed penetration wounds at 4 o'clock about 3 mm. from the limbus, a central perforating wound and a third perforation at 11 o'clock about 2 mm. from the limbus—all the corneal wounds having a prolapse of iris. The anterior chamber was filled with blood.

The patient was placed under treatment with 40,000 units of penicillin every three hours, and tetanus and gas gangrene antitoxin U. S. P. was administered.

The initial surgical treatment, undertaken four hours later, consisted of the following procedures: right eye: excision of the prolapsed iris; left eye: (1) excision of the prolapsed iris, (2) suture of corneal wounds and (3) limbal incision for (*a*) evacuation of the hyphema and (*b*) evacuation of loose lenticular material.

The following day the right eye appeared in good condition, with a clear anterior segment, although there was some vitreous haze. The left eye showed an intense inflammatory reaction, with clouding of the aqueous.

On the second postoperative day, July 16, examination of the right eye showed a clear anterior segment, but the vitreous was more turbid and details of the fundus could not be seen; vision was reduced to counting fingers at 3 feet (90 cm.). The left eye showed frank endophthalmitis, with purulent exudate extending through the anterior chamber. The patient was taken to the operating room for the following procedures: (1) irrigation of the anterior chamber of the right eye with penicillin solution (5,000 units per cubic centimeter), and (2) simple enucleation of the left eye with drainage. Cultures of material from the enucleated eye were made.

On July 18, vision in the right eye was reduced to perception of hand motions, the anterior segment and lens continued to be clear, but yellow exudate was grossly visible behind the lens; episcleral injection was becoming pronounced, and the globe was tender. Smears from the enucleated eye revealed no organisms, but the culture was reported as showing a gram-negative bacillus.

Since the response to penicillin was poor, both as given systemically and as injected into the anterior chamber, systemic administration of streptomycin [2] (0.5 Gm. every four hours) was begun, and, at the suggestion of Leopold,[3] approximately 900 micrograms of streptomycin was injected into the vitreous. For the latter, a tuberculin syringe and a 26 gage needle were used, the needle being directed through the pars plana in the upper nasal area.

On the following day, July 19, the clinical appearance was worse, and vision was reduced to vague perception of hand motions. The intravitreal injection was repeated in larger dose (approximately 1,400 micrograms), and a streptomycin pack, containing 20,000 micrograms per cubic centimeter, was placed in the cul-de-sac for one hour.

Four days later, July 23, vision was reduced to nil—the patient did not have light perception. The clinical appearance of the eye remained in status quo except that a cataract could be seen developing, the opacity extending forward from the posterior subcapsular area.

On July 26, six days after the intravitreal injection, the inflammatory reaction was becoming less marked, although there was still absence of light perception. Systemic administration of streptomycin was discontinued.

By July 30, the tenth day after the injection, light perception had returned; the inflammatory reaction of the globe was subsiding, and the lens had become irregularly opaque posteriorly.

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2. The streptomycin used was calcium chloride complex.®

3. Leopold, I. H.: Personal communication to the author.

The patient was discharged from the hospital on August 9, to the care of Dr. George Dublin, at Wills Hospital, Philadelphia. The eye at this time was almost white; the anterior chamber was grossly clear; the lens was opaque posteriorly, and light perception and projection were good temporally, though impaired nasally.

The subsequent history is briefly summarized: The patient was admitted to Wills Hospital on Aug. 12, 1947, for a series of treatments with artificial fever, induced with intravenous injections of typhoid vaccine. He was discharged one month later and was readmitted October 7, when a linear cataract extraction was done.

The patient was seen again in April 1948. The cornea showed scattered small, punctate scars. The anterior chamber was clear. There was a small surgical coloboma. The eye was aphakic. A narrow, dense white membrane stretched across the center of the pupillary space. Except for a single opaque strand in the retrolental area, the vitreous was clear. The nasal, superior and inferior periphery of the retina appeared normal. Beginning at the somewhat pale disk and extending in a fan-shaped area temporally a gray-white, cobweb-like scar could be seen. The scar tissue appeared to be retinal, covering some of the vessels; in other areas, the vessels coursed over the scar. This scar formation included the macula and a rather large perimacular area.

The patient fixed eccentrically—the eye was held in about 15 degrees of exotropia—and with a + 12 D. lens visual acuity varied from 16/200 to 20/200, according to the searching attempt at fixation.

COMMENT

A rather interesting part of the clinical picture was the complete loss of light perception for six days. This may have been the result of acute optic neuritis, either toxic or due to direct bacterial infection of the nerve head itself. At the time of writing, the fundus picture showed a somewhat pale nerve head, partially covered with a strandlike white membrane.

The subsequent retinal degeneration in this case parallels that observed in animal experimentation with streptomycin, except that it was not localized at the site of injection. However, it should be pointed out that a total of 2,300 micrograms of streptomycin was placed in the posterior segment and that the same amount introduced experimentally into animal eyes might cause widespread chorioretinal degeneration.

It is felt that direct intravitreal injection of streptomycin in this case saved one eye after systemic therapy with penicillin had failed. Later bacteriologic reports [4] showed that the infecting organism was a gram-positive, spore-forming bacillus of the brevis group. Sensitivity tests [5] showed the organism to be more susceptible to penicillin than to streptomycin in vitro. The clinical result stresses the inadequacy of systemic routes of administration for infections of the vitreous humor and the effectiveness of local therapy, even when the antibiotic

4. Morton, H.: Personal communication to the author.

5. Sensitivity tests were made by Mr. R. N. Shoemaker, research fellow in the department of biology, Lehigh University.

used has a lesser degree of antibacterial activity. It may be that immediate intravitreal injection of penicillin or streptomycin, or perhaps, even better, a combination of the two, would have changed the course of events in the left eye.

SUMMARY

Intravitreous injection of streptomycin was used clinically in a case of bacterial endophthalmitis and appears to be a safe procedure in cases in which it is indicated. Unfavorable effects on the vitreous were practically nil. Retinal degeneration occurred, as in experimental animals, but one could minimize this by not exceeding the recommended dosage.

1248 Hamilton Street.

Clinical Notes

A SIMPLIFIED PERIMETER OF WALL TYPE

ANTHONY AMBROSE, M.D.
NEWARK, N. J.

For the simplified wall perimeter which I present I claim nothing original except the idea for the wall suspension.

The wall clamp was taken from an old gynecology table. The supporting bar was made by a blacksmith. Both pieces were chrome plated. The perimeter arm is ¾ inch (1.9 cm.) plywood and is graduated to measure 100 degrees. It was given four coats of jet black paint. I had previously put on four coats of a neutral gray but found that the black paint is much more satisfactory. The point on the end of the arm was a brass cup hook which was straightened out and filed to a point. It points directly on the protractor to the meridian which is being examined. A wooden drawer knob has been screwed onto the back of the arm in order that one may hold it in position by hand in the oblique angles. The protractor is made of the same material and at first was 6 inches (15 cm.) in diameter, but I later found that I had to cut the sides off, as the width prevented the instrument from lying flat against the wall.

The right-angled supporting arm is made of the same plywood as is the T-shaped foot plate, which is adjustable. The end of the supporting bar was flattened, and three holes were drilled in it: One is to accommodate a toggle bolt, which serves to connect the perimeter arm, the protractor and the supporting arm. The latter and the protractor are screwed together by screws placed in the other two holes. The wing of the toggle bolt is screwed into the back of the perimeter arm. The toggle bolt is secured by two washers and a butterfly nut at its very end. The head of the toggle bolt was dipped in flat white paint six times, being dried between each dipping. It serves as a fixation point. I marked the degrees off each side of the arm with raised numbers used for identifying window screens, starting at 10 degrees with no. 1 and ending with 90 degrees with no. 9, the zero point being opposite, on the line of the fixation point.

I first used the perimeter with the protractor fixed to the supporting bar and employed a Bausch & Lomb chin rest, which I use for the tangent screen. I later bought and attached the supporting arm when I was able to secure a Bausch & Lomb chin rest from a Ferree-Rand perimeter. The moving parts are separated from one another by washers from the wheels of roller skates. I use Dr. Berens' test objects attached on dowels 18 inches in length and ¼ inch

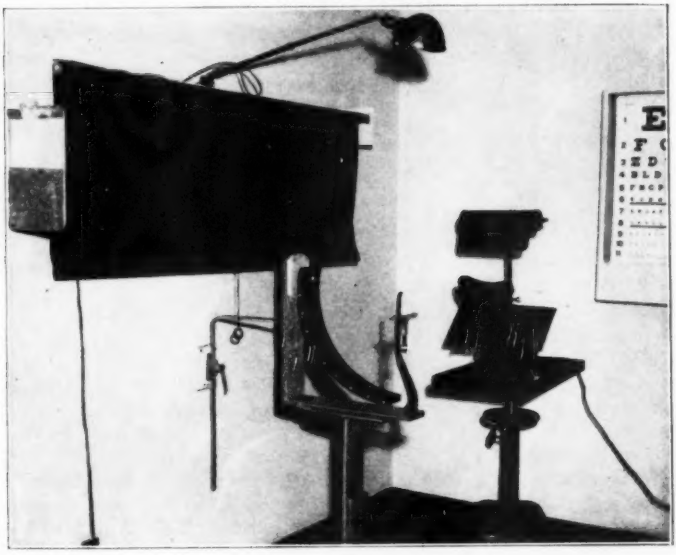

Fig. 1.—Instrument in position of use.

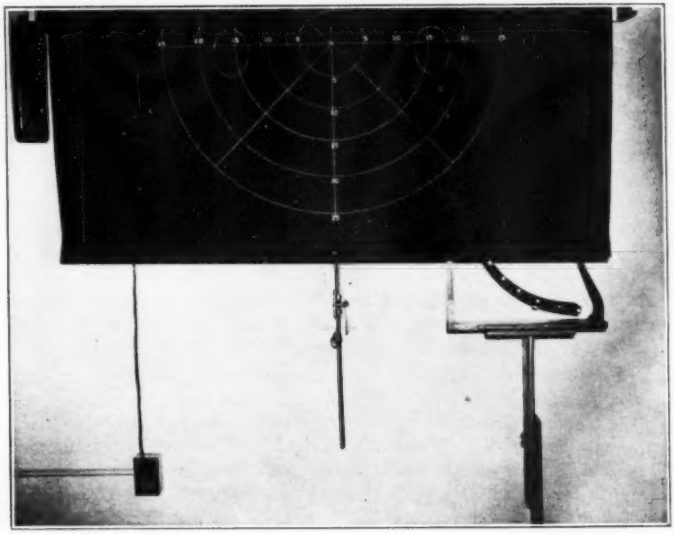

Fig. 2.—Instrument flat against the wall, partly covered by the tangent screen.

(0.63 cm.) in thickness, painted the same black as that of the perimeter. When taking the visual field, I pull down my tangent screen, which is black and offers the same background as the perimeter arm. When the peripheral fields are finished, I move the patient back to 1 meter and use a Bausch & Lomb chin rest, which I have

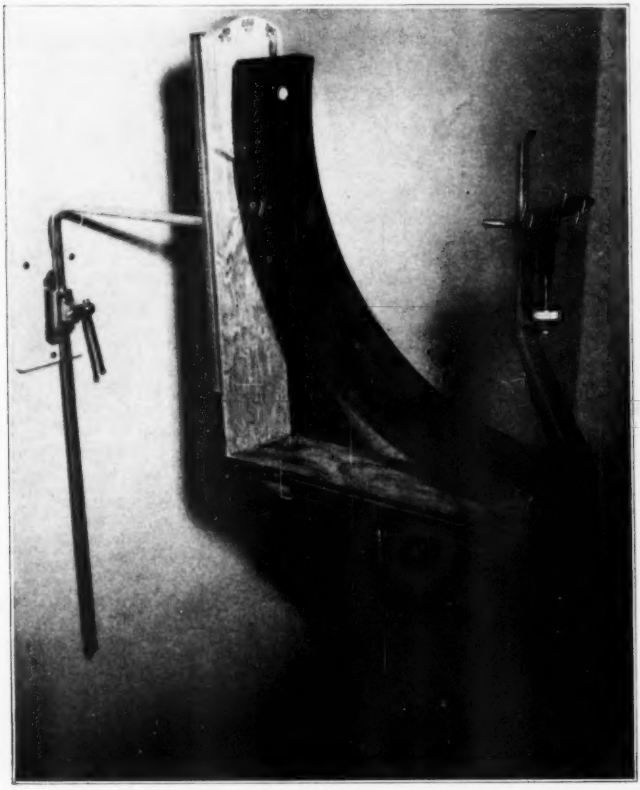

Fig. 3.—Close-up view of the instrument.

on a movable pedestal, in taking the central fields. When the occasion requires it, I also use the Bausch & Lomb stereocampimeter, as shown in the pictures. The lighting is obtained from an overhead lamp, which illuminates the tangent screen. It is a 100 watt daylight bulb, the illumination being augmented from the side by another daylight bulb.

In my opinion, the instrument has many advantages. It is cheap; it can be put behind a door, or even inside a closet. It can be permanently attached by the supporting arm to a wall or a door, and the patient is then adjusted by a revolving stool. It might also be attached to a table by a bolt on the lower supporting arm.

I conceived the idea because my Ferree-Rand perimeter took up more space than was available in the room in which I was using it.

NOTE.—Since the illustrations were made, a floor foot plate, 12 by 4 by 1 inch (30.4 by 10 by 2.5 cm.), was attached to the upright support in order to give the instrument more stability.

15 Washington Street.

News and Notes

GENERAL NEWS

The American Orthoptic Council.—The American Orthoptic Council announces the second annual course of instruction for orthoptic technicians. This course consists of two parts, the first, nine weeks of lectures, demonstrations and laboratory work by outstanding ophthalmologists and certified technicians, from June 25 to Aug. 27, 1949, at Nasson College, Maine.

This basic instruction will be followed by the second part, which consists of six to twelve months of practical work in clinics and offices, throughout the United States, under the supervision of certified orthoptic technicians. Completion of the full course will qualify the student to take the examinations of the American Orthoptic Council. Further information may be procured from the American Orthoptic Council, 1605 Twenty-Second Street, N.W., Washington 8, D. C.

Attention Candidates for Board Examinations.—The American Board of Ophthalmology wishes to announce that it does not evaluate, approve or disapprove any ophthalmic residency toward fulfilling the requirements of candidates for board examinations. Any candidate who qualifies for the board examination and completes the prerequisites as outlined in the booklet of information will be accepted. A copy of this booklet can be obtained from the Secretary of the American Board of Ophthalmology, 56 Ivie Road, Cape Cottage, Maine.

The Annual deSchweinitz Lecture.—The Twelfth Annual deSchweinitz Lecture will be given on Thursday, Nov. 17, 1949, by Arthur J. Bedell, M.D., of Albany, N. Y. His subject will be "The Macula in the Aged."

SOCIETY NEWS

Annual Congress of the Ophthalmological Society of the United Kingdom.—The annual congress of the Ophthalmological Society of the United Kingdom was held at the Royal Society of Medicine, 1 Wimpole Street, London, W.1, on March 31 and April 1 and 2, 1949; F. A. Juler, C.V.O., M.B., F. R. C. S., president.

The presidential address, entitled "Some Points in the Operation for Acute Glaucoma" and "Reflections on Refraction," was followed by the presentation of the Bowman medals.

The following papers were presented: "The Technic of Plastic Operations in the Neighborhood of the Orbit," Mr. D. N. Matthews; "Reduction of Intraocular Tension by Curare, Retrobulbar Injection of Procaine and Di-Isopropyl Fluorophosphate," Mr. J. R. Wheeler; "The Problem of Awareness or Nonawareness of Visual Field Defects," and "Cerebral Metamorphopsia," Dr. Macdonald Critchley; "Normal and Pathologic Ocular Pigment," Mr. Eugene Wolfe; "Clinical Estimation

of Pressure in the Retinal Arteries," Dr. E. Hartmann; "Aneurysms of the Internal Carotid Artery," Dr. S. P. Meadows; "Congenital Total Color Blindness, with Otosclerosis and Hypertension as Associated Hereditary Abnormalities," Mr. W. J. Wellwood Ferguson and Dr. Alastair G. MacGregor; "Measurement of the Retrobulbar Resistance (Orbitonometry) in the Clinic," Dr. A. C. Copper; "Clinical Electroretinography," Dr. G. Karpe; "Problems in Ophthalmic Dispensing," Mr. J. Pike; "Retinal Arteriolar Spasm in Toxemia of Pregnancy," Dr. J. Berkson.

A discussion on "Corneal Grafting" was opened by Prof. A. Franceschetti; Mr. J. W. Tudor Thomas; Prof. G. P. Sourdille, Mr. B. W. Rycroft and Mr. D. P. Choyce.

Brief pictorial demonstrations of cases were made.

Medical Society of the State of New York, Section on Ophthalmology.—The annual convention of the Medical Society of the State of New York, Section on Ophthalmology, was held May 5 at the Hotel Statler in Buffalo. The chairman of the program was Darrell G. Voorhees, M.D., of New York; the secretary, Walter F. Duggan, M.D., of Utica. The following papers were presented: "Complications and Failures of Retinal Reattachments," by Ivan J. Koenig, M.D., Buffalo; "Functions of the New York State Commission for the Blind," by David F. Gillette, M.D., Syracuse, and "Defects in the Visual Fields Resulting from Increased Intracranial Pressure," by C. Wilbur Rucker, M.D. (by invitation), of Rochester, Minn. Discussions were opened by Loren P. Guy, M.D., New York; David F. Gillette, M.D., Albany, and John F. Gipner, M.D., Rochester.

Ophthalmology Lectures, Royal College of Surgeons of England.—The following lectures were delivered at the College, in Lincoln's Inn Fields, London, W.C.2, on March 29 and 30, 1949: "Cataract Associated with Lesions of the Skin," Prof. A. Franceschetti, University of Geneva; "Ophthalmic Aspects of Protein Deficiency and Disordered Protein Metabolism," Prof. G. B. Bietti, Pavia University; "Psychosomatic Symptoms in Ophthalmology," Dr. E. Hartmann, Hôpital Lariboisière, Paris; "Ophthalmic Manifestations of Besnier-Boeck Disease," Prof. H. J. M. Weve, Rijksuniversiteit.

Oxford Ophthalmological Congress.—The next meeting of the Oxford Ophthalmological Congress will be held in Oxford, England, July 7 to 9, 1949. The Doyne Memorial Lecture will be delivered at this meeting by Professor Goldman, of Berne, Switzerland. The main discussion will be the "Principles and Practice in Maintaining Asepsis During Ophthalmic Operatons."

Further information may be procured from the honorable secretary and treasurer, I. C. Fraser, 12 St. John's Hill, Shrewsbury, Shropshire, England.

The Ophthalmological Society of Australia.— At the annual meeting, held in the first week of October, the following officers were elected: president, Dr. Arthur H. Joyce; vice president, Dr. E. J. McGuinness; honorary treasurer, Dr. A. E. F. Chaffer; honorary secretary, Dr. A. L. Lance, 27 Commonwealth Street, Sydney.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Aqueous Humor

PARASYMPATHOMIMETIC EFFECT OF AQUEOUS HUMOR IN HUMAN EYES WITH AND WITHOUT CHRONIC SIMPLE GLAUCOMA. S. BLOOMFIELD, Proc. Soc. Exper. Biol & Med. **60**: 293, 1943.

The results are presented of the bioassay of aqueous humor from human eyes prepared according to the method applied by Engelhart to animals. In a series of 10 human eyes without glaucoma, every sample of aqueous humor contained a parasympathomimetic substance which, in the 2 cases so tested, was found to be similar to acetylcholine. In the aqueous humor of 7 human eyes with chronic simple glaucoma no such parasympathomimetic substance could be demonstrated.

W. ZENTMAYER.

A NEW METHOD OF MEASURING THE RETINAL BLOOD PRESSURE AS AN OBJECTIVE PROOF OF THE FORMULA OF THE HYDRODYNAMIC EQUILIBRIUM OF THE EYE. A. DASHEVSKY, Vestnik oftal. **26**: 22, 1947.

In a previous paper Dashevsky described a formula expressing a new law of the adequate reaction of the eye to pressure which is in direct proportion to the difference of the diastolic blood pressure and the true intraocular pressure.

In order to verify the correctness of his formula of the hydrodynamic equilibrium of the eye, Dashevsky succeeded in measuring the diastolic blood pressure in the eye without using the usual tonoscopic method (without increasing the ophthalmotonus to the level of the diastolic pressure or the appearance of the first pulsation of the central retinal artery). The method is an indirect one, which combines the reactivity of the eye, the opthalmotonus and the blood pressure, and it opens new prospects for experimental work.

This formula combines not only the hydrostatic relationship of the blood pressure, the ophthalmotonus and the physicochemical condition, but also the important nervous component, the changes of which appear as the variations in the reactivity of the eye. The law of the adequate reaction of the eye to its pressure is the result of the mobile, and at the same time stable, condition in the eye which is called hydrodynamic equilibrium.

A table and the explanation of the formula illustrate the article.

O. SITCHEVSKA.

Bacteriology and Serology

A Comparison of Aniseikonic Test Instruments and Prolonged Induction of Artificial Aniseikonia. P. W. Miles, Am. J. Ophth. **31:** 687 (June) 1948.

Miles states that artificially produced aniseikonia causes distortion of objects, interferes with vision and, if the size difference is more than 5 per cent, prevents fusion and stereopsis altogether. He describes experiments in which meridional magnifying lenses were worn for prolonged periods. W. S. Reese.

Congenital Anomalies

Crater-Like Holes in the Optic Disc. E. Rosen, Brit. J. Ophth. **32:** 465 (Aug.) 1948.

Rosen describes and pictures 7 cases of holes in the optic disk. Such holes may erroneously be regarded as evidence of glaucomatous changes, particularly when there are pupillary inequalities, atrophy of the iris or field defects. These holes may also be present in amblyopic eyes, in which instance recognition should lead to avoidance of occlusion therapy. The field defect may be rather constant and may be recognized by an observant patient. The possibility that such a "pit" will extend back into the orbit and unite with a cyst, thus producing unilateral exophthalmos, should also be borne in mind. W. Zentmayer.

Cornea and Sclera

Stimulation of Corneal Epithelization with Topical Application of Erythrocytes. F. W. Newell, Am. J. Ophth. **30:** 1238 (Oct.) 1947.

Newell found that treatment of experimentally abraded corneas with an ointment containing washed, packed human red blood cells resulted in significantly increased rates of epithelization in the guinea pig. W. S. Reese.

Cyanide Inhibition of Corneal Respiration. W. A. Robbie, P. J. Leinfelder and T. D. Duane, Am. J. Ophth. **30:** 1381 (Nov.) 1947.

Robbie, Leinfelder and Duane found that corneal respiration is almost completely inhibited by 10^{-3} molar solution of hydrogen cyanide, but that recovery from exposure to cyanide is rapid. W. S. Reese.

Corneal Grafts in the Child and the Adolescent. G. E. Jayle, Arch. d'opht. **7:** 148, 1947.

The author reports a case of corneal graft in a child aged 11 who had typical interstitial keratitis with extensive vascularization. He reports a second case of such a graft in an adolescent aged 16, who had bilateral amblyopia due to a leukoma of the cornea, resulting from ophthalmia neonatorum. The author describes his technic. In the first case glaucoma developed approximately six weeks after the operation and was controlled by trephining. About fifteen days after operation

there had been an anterior synechia, which was freed without incident. As the result of the development of glaucoma in this case, the author advocates trephination prior to the corneal grafting. In the second case, in which there was a strong nystagmus, the graft was successful, with some improvement in vision. These cases are of interest from two points of view: First, it is possible to carry out this procedure in young subjects, and, second, the process of growth does not interfere with the obtaining of a good result. He had come, therefore, to believe that a delay of more than three years is not indicated.

S. B. MARLOW.

CORNEAL GRAFTS IN TWO PATIENTS WITH GROENOW'S DISEASE. E. HARTMANN and P. V. MORAX, Bull. Soc. d'opht. de Paris, March-April 1947, p. 121.

Usual treatment, including the wearing of contact lenses, did not in any way change the progress in either patients with nodular disease of the cornea. Seven months after the corneal transplantation, the vision of the first patient had increased from 1/25 to 1/3. In about the same length of time a transplant gave the second patient an increase in vision of from 1/25 to 1/10. Spots in the posterior portion of the cornea were still visible with the slit lamp in each eye seven months after the operation, but there seemed to be no increase in size of these dots.

L. L. MAYER.

CORNEAL CHANGES DURING TREATMENT WITH ARSPHENAMINE. T. A. J. VAN DOORMAAL, Nederl. tijdschr. v. geneesk. **91:** 2751 (Sept. 27) 1947.

According to van Doormaal, treatment with arsphenamine preparations may cause serious corneal lesions. He describes the case of a man aged 47 in whom, during treatment with arsphenamine and a bismuth compound for syphilis, there developed severe dermatitis, conjunctivitis and bilateral corneal ulcers with perforation. The patient recovered slowly from his dermatitis and became almost blind. Corneal lesions which develop during treatment with arsphenamine usually, but not always, appear in the course of arsphenamine dermatitis.

J. A. M. A. (W. ZENTMAYER.)

Experimental Pathology

EFFECTS OF NITROGEN MUSTARD ON THE PERMEABILITY OF THE BLOOD–AQUEOUS HUMOUR BARRIER TO EVANS BLUE. H. DAVSON and J. P. QUILLIAM, Brit. J. Ophth. **31:** 717 (Dec.) 1947.

The work described was undertaken to find out whether the rate of penetration of Evans blue into the eye could be used as an index of the severity of a lesion caused by nitrogen mustard (methyl-bis-[B-chloroethyl]-amine hydrochloride), and to this end the effects of three preparations of the substance, known to have different toxicities, were compared. The results showed that this was indeed possible; moreover, an extremely interesting dependence of the severity of the lesion in one

eye on the condition of the other eye became manifest; for this reason, the part of the work bearing on this point is being published.

It is well known that the permeability of the capillary endothelium to proteins, and therefore to Evans blue, is largely determined by the physiologic state of the capillaries; if they are dilated, their permeability is high; if contracted, it is low. If the lesion produced by a high concentration of nitrogen mustard in one eye causes a reflex dilatation of the vessels in the iris of the other, then the phenomena described here are explicable on the basis of reflex action. In confirmation of this statement, it has been noted that after instillation of nitrogen mustard into the left eyes of a series of animals a ciliary injection was observed in the untreated (right) eye; only on one occasion, however, was it possible to demonstrate that injected Evans blue appeared in the contralateral eye. One may conclude, therefore, that a severe lesion in one eye potentiates the action of a mild nitrogen mustard agent in the other by reflex action; in the present case, the effects of this potentiation are greater with the milder than with the stronger solution.

W. ZENTMAYER.

General

VIRUS STUDIES IN LYMPHOMATOID DISEASES OF THE OCULAR ADNEXA. A. E. BRALEY and R. C. ALEXANDER, Am. J. Ophth. **30:** 1369 (Nov.) 1947.

Braley and Alexander present a preliminary report of a new virus. This virus was obtained from lymph nodes and the submaxillary gland of a patient with a form of rapidly progressive exophthalmos. The virus produces encephalitis in rabbits, guinea pigs and mice and grows well in tissue culture.. The cellular response to the virus in animals is predominantly lymphocytic. The virus is submicroscopic. It is neutralized by blood serum from the patient. Normal human serum and the blood serum of most laboratory animals contain no neutralizing antibodies. The virus has not been identified in any known classification.

W. S. REESE.

READING DIFFICULTY (DYSLEXIA) FROM THE OPHTHALMIC POINT OF VIEW. G. E. PARK, Am. J. Ophth. **31:** 28 (Jan.) 1948.

Park concludes that dyslexia is an entity and is sufficiently common to require attention. Its correction requires study of the child from the physical, emotional and pedagogic points of view. He makes a somewhat detailed analysis of the ophthalmic findings that were coincidental with other symptoms in a series of 133 cases of dyslexia.

W. S. REESE.

COMPARISON OF EYE CONDITIONS AMONG 1,000 READING FAILURES, 500 OPHTHALMIC PATIENTS, AND 150 UNSELECTED CHILDREN. T. H. EAMES, Am. J. Ophth. **31:** 713 (June) 1948.

Eames reports his observations in a comparative study of the ocular conditions of 1,000 poor readers, 500 patients with ophthalmic disorders and 150 unselected children. His study indicates that for the present group at least hypermetropia, exophoria at the reading distance, retarded

speed of work recognition and intelligence quotients below 90 occur more frequently among poor readers than in the other groups tested, but that the median amount of defectiveness is not appreciably greater in any of the groups. This conclusion is in line with the clinical observation that poor readers are often troubled to a greater extent than others by such handicaps as low degrees of hypermetropia and other ocular defects.

W. S. REESE.

NEW CONCEPTS CONCERNING OCULAR COMPLICATIONS FOLLOWING VACCINATION. E. ROSEN, Ophthalmologica **115:** 321 (June) 1948.

In the spring of 1947 mass vaccinations against smallpox were performed in New York city. Ocular complications were seen from six to twelve days after the vaccination. They included interstitial keratitis associated with vestibuloauditory symptoms, metaherpetic keratitis, dendritic keratitis, exudative chorioretinitis, central serous retinopathy, iritis and panophthalmitis, thrombophlebitis and lesions of the extraocular muscles. The lesions of the retina, such as edema, endophlebitis, perivasculitis and neuritis, are closely related to the changes in the brain found in postvaccinal encephalitis. The literature on this subject is reviewed.

H. P. KIRBER.

General Diseases

SCLERODERMA AND LESIONS IN THE FUNDUS. E. HARTMANN, P. COLLIN and P. VERGNE, Ann. d'ocul. **181:** 220 (April) 1948.

The authors present the case of a patient with scleroderma and an unusual lesion in the fundus of each eye. The posterior poles of both eyes were seeded with bright spots of varying size, shape and color. These spots were not confined to the distribution of the retinal vessels, and they diminished in number toward the periphery. With the binocular ophthalmoscope, they appeared to be deep, and the retina did not seem to be elevated over the lesions. In the right eye the macula was involved, though corrected vision was 10/10. The macula in the left eye was clear, and vision was 7/10. The visual fields and retinal arterial pressure were normal.

Clinically the spots appeared much like drusen; but, because of the patient's youth and the abundance of the lesions, the authors do not feel that the changes were typical of drusen. They believe that the lesions were caused by a disturbance in Bruch's membrane similar to that in drusen, but that in their case the changes were related to the generalized scleroderma.

P. R. MCDONALD.

ACUTE OCULAR MANIFESTATIONS OF ARIBOFLAVINOSIS. H. J. STERN, Ophthalmologica **114:** 103 (Aug.) 1947.

If the vessels of the limbal plexus throw out new capillaries, a diagnosis of riboflavin deficiency can be made in the presence of any primary corneal lesion. A case is presented in which the diet was grossly deficient in riboflavin and recovery occurred promptly with riboflavin therapy.

F. H. ADLER.

Glaucoma

A Statistical Study of Glaucoma. J. C. Holst, Am. J. Ophth. **30:** 1267 (Oct.) 1947.

Among 12,127 admissions to the University eye clinic in Oslo, Norway, were 2,024 patients, or 8.4 per cent, with glaucoma simplex; 1,261 patients, or 62.3 per cent, were men, and 763 or 37.7 per cent, were women. The fact that men greatly outnumbered women is the more surprising, as in the age group (over 50) in which the incidence of glaucoma is the highest the percentage of men to women is 45.5 : 54.5.

Hypermetropia was present in 25 per cent of patients with glaucoma simplex; emmetropia, in 50 per cent, and myopia, in 19 per cent; 5 per cent were astigmatic. Inverse astigmatism was found in as great a proportion as 2 per cent. Of 459 patients examined for exfoliation of the lens capsule, the lesion was present in 375 (82 per cent).

Of 53 patients with unilateral glaucoma in whom exfoliation was found only on one side, it was always in the eye with the glaucoma. Exfoliation in the healthy eye, but not in the glaumatous eye was never observed.

W. Zentmayer.

The Clinical Use of Di-Isopropyl Fluorophosphate (DFP) in Chronic Glaucoma. W. G. Marr, Am. J. Ophth. **30:** 1423 (Nov.) 1947.

Marr concludes that di-isopropyl fluorophosphate has little chance of success in cases in which the commonly used miotics fail and that the drug is not always innocuous.

W. S. Reese.

Reoperation for Glaucoma. P. C. Kronfeld, Pennsylvania M. J. **51:** 148 (Nov.) 1947.

In about 20 per cent of unsuccessful trephine operations by gonoscopic examination the trephine opening proved to be plugged on the inside by the ciliary body, lens or iris. In about 80 per cent there was closure of the outer aperture of the trephine canal.

Not more than 20 per cent of second trephinations were successful. The most favorable site for the second operation seemed to be in the horizontal meridian. A typical sequence of surgical procedures is described, starting with an external filtering operation and followed, if necessary, by one or two cyclodialyses, which are followed, if necessary, by one of two cyclodiathermies. This sequence of operations is capable of normalizing the ocular tension in 85 per cent of chronic simple, wide angle glaucomas

W. Zentmayer.

Glaucoma Secondary to Fibrocystic Disease of Bone. J. W. E. Cory, Brit. J. Ophth. **31:** 731 (Dec.) 1947.

A farmer aged 58 complained of loss of vision and discharge from the left eye. For at least forty years there was a swelling over the left temporal region.

The left eye showed slight proptosis and vision was 6/60. Intraocular pressure was 33.75 mm. of mercury. The optic disk was cupped. The field of vision was restricted to a small area in the upper and outer quadrant. Roentgenograms showed a honeycombed condition of bone

in the left frontal, temporal and occipital bones. The sphenoid was fully involved. The orbital fissure could not be demonstrated; the frontal and maxillary sinuses were obliterated. The only other bones affected were the left side of the mandible and the lower third of the right humerus.

A corneoscleral trephining of the left eye was done. The author thinks there is little doubt that the ophthalmic condition was due to the abnormal bony formation. W. ZENTMAYER.

Instruments

SIZE OF LINE IN THE MADDOX-ROD TEST. R. G. SCOBEE and E. L. GREEN, Am. J. Ophth. **31:** 697 (June) 1948.

Scobee and Green conclude that variation in measurements of heterophoria is not due to variations in the size of the line produced by different-sized muscle lights. W. S. REESE.

SOME PROBLEMS IN THE CALIBRATION OF TONOMETERS. JONAS S. FRIEDENWALD, Am. J. Ophth. **31:** 935 (Aug.) 1948.

Friedenwald presents a preliminary report on the calibration of tonometers. He finds that the calibration scales of Schiøtz and McLean are both too high and states the belief that the average normal intraocular pressure is between 18 and 19 mm. of mercury. He discusses ocular rigidity and estimates the coefficient of the average normal eye as 0.0245, corresponding to an increase of 5.8 per cent in the intraocular pressure for a displacement of 1 cu. mm. of fluid. W. S. REESE.

A LOW POWER INFRA-RED MICROSCOPE. T. STUART-BLACK KELLY, Brit. J. Ophth. **32:** 396 (July) 1948.

Kelly describes a low power infra-red microscope. The viewing device can replace the normal binocular microscope on a slit lamp table. Incorporated in the microscope is an infra-red converter tube. Considerable density of cornea can be penetrated. A contact glass improves penetration of a rough surface. Penetration of cataract seems to depend on the chemistry of the cataract. W. ZENTMAYER.

A SIMPLE, SELF-REGISTERING PERIMETER. W. WEIDMANN, Ophthalmologica **115:** 332 (June) 1948.

The perimeter consists essentially of a hollow sphere made of transparent plastic material, a self-registering mechanism and a projector for the test object, which appears as a spot of light on the outside and the inside of the sphere. The instrument is simple and is claimed to be inexpensive. It is manufactured in Switzerland. H. P. KIRBER.

Lens

INTRACAPSULAR EXTRACTION OF CATARACT. C. DUVERGER and P. BREGEAT, Arch. d'opht. **7:** 379, 1947.

The authors emphasize the advantages which a keratome incision with enlargement by scissors affords. The suture is described, and the value of a good capsule forceps and the use of the left hand in the pro-

duction of pressure during extraction is pointed out. The method of suturing by half-knots is described; finally, the precautions necessary in regard to the iris and the incidence of loss of vitreous are indicated. The authors' procedure is described in some detail.

S. B. MARLOW.

CONNECTION BETWEEN THE POSITION OF ZONULAR OPACITIES IN THE LENS AND THE TIME OF THEIR FORMATION ESTIMATED FROM SIMULTANEOUSLY OCCURRING ENAMEL HYPOPLASIA. A. HUGGERT, Acta ophth. **26:** 7, 1948.

There is a diversity of opinion in regard to the time of formation of the various layers of the lens that constitute the zones of optical discontinuity. The author examined a number of zonular cataracts, took measurements of their size, noted their position in the lens and correlated these observations with the probable time of onset of a coexisting enamel hypoplasia. The examinations show that the lenticular layer of the outer embryonic nucleus is established at the time of birth while the layer within the innermost part of the adult nuclear zone is probably established between the age of 1 and 2 years.

O. P. PERKINS.

Lids

CORRECTION OF PTOSIS BY TUCKING OF THE LEVATOR. A. GARDILCIC, Ophthalmologica **115:** 269 (May) 1948.

The advantages and disadvantages of accepted procedures for the correction of ptosis are discussed, and the literature is reviewed. Gardilcic proposes to expose the levator from the outside, then anchor three double-armed sutures in the muscle fibers and attach these to the anterior surface of the tarsal plate, thus effecting a tucking and advancement of this muscle. In cases of total ptosis, the tarsal plate is exposed extensively, and the sutures are attached to it close to the lid margin. To prevent an eversion of the upper lid, additional sutures are placed through the tucked muscle and the upper margin of the tarsal plate. The advantages claimed for this procedure are as follows: 1. The amount of correction can be varied by anchoring the sutures at various levels of the muscle and by attaching them at different levels to the tarsal plate. 2. There are no anatomic derangements, and the procedure can be repeated if necessary. 3. The technic is fairly simple.

The procedure is recommended for partial, as well as for total, ptosis.

H. P. KIRBER.

Ocular Muscles

THE VERGENCE TEST: AN EVALUATION OF THE VARIOUS TECHNIQUES. W. H. FINK, Am. J. Ophth. **31:** 49 (Jan.) 1948.

Fink concludes that the vergence test is an important part of the ophthalmologist's daily routine. It is generally admitted that the various technics used for this test do not give consistent results. An attempt is made to determine which is the most efficient and the most dependable. Certain changes in technic seem to increase the efficiency of the test. These changes in technic, according to the data, produce more dependable readings, cause less fatigue to the patient, make the test more understandable to the patient, save time for the examiner and give a more correct interpretation of the findings.

W. S. REESE.

TREATMENT OF PHORIAS IN ADULTS. E. HEALY, Am. J. Ophth. **31:** 703 (June) 1948.

Healy concludes that phorias respond readily to treatment and that the aim should be relief of symptoms and not orthophoria.

W. S. REESE.

PROBLEMS IN RESEARCH IN ORTHOPTICS. F. E. JACKSON, Am. J. Ophth. **31:** 805 (July) 1948.

Jackson concludes that much time and preliminary effort involved in research can be minimized by (1) a definite system in keeping records of diagnosis, treatment and follow-up observations on cases, (2) an abstract file of current publications and (3) a diagnostic file of case histories. Analysis of cases represents the bulk of orthoptic research. Results of such analysis can be presented in three ways: as a statistical survey, as a comparative study and as a report of individual cases.

Five benefits are to be derived from research in orthoptics: (1) clarification of orthoptic terminology, (2) standardization for evaluation of results, (3) elimination of variable factors, (4) collection of sensory data and (5) a better sense of perspective for routine treatment.

W. S. REESE.

Parasites

HYDATID OF THE ORBIT. H. HOLLAND, Brit. J. Ophth. **32:** 395 (July) 1948.

Holland has seen 8 cases of hydatid cyst of the orbit. The cyst is generally on the nasal side and always in the upper fornix. In the early stage there is some fulness of the upper fornix, but in the later stages proptosis is so extreme that the eye cannot be closed. Vision is usually good. The diagnosis can be confirmed by aspiration of the contents of the tumor and examination for hooklets after the patient has been prepared for operation. If hooklets are found, the needle should be left in place and the cyst excised at once.

W. ZENTMAYER.

CHRONIC SUPERFICIAL PUNCTATE KERATITIS CAUSED BY THE ONCHOCERCI VOLVULUS. M. APPLEMANS, Ophthalmologica **114:** 129 (Sept.) 1947.

The case histories of 2 patients with ocular onchocercosis are reported, and the author stresses his belief that a diagnosis of onchocercosis is possible only when the presence of the mobile larvae is confirmed by biomicroscopy. It is not sufficient evidence that one obtains a history of the patient's having been in the tropics and of having had a chronic superficial punctate keratitis or a uveitis with eosinophilia demonstrated in the blood. The parasites must be found in the eye. The mere presence of the larvae of Onchocerca volvulus or Onchocerca caecutiens in the anterior chamber is not sufficient to produce iritis, but an allergic factor must also play a part in the origin of the keratitis and the uveitis. The only form of treatment known is the extirpation of the filaria nodules. This prevents the development of the embryos and hinders the entrance of the larvae into the eye as long as the carrier is guarded against new infection. The author recommends application

of an ointment containing 5 per cent mild mercurous chloride U. S. P. in the conjunctival sac in those cases of superficial punctate keratitis caused by filariasis in which parasitic tumors are not present.

F. H. ADLER.

Pharmacology

OCULAR EFFECT OF SEVERAL IRRITANT DRUGS APPLIED DIRECTLY TO THE CONJUNCTIVA. J. J. ESTABLE, Am. J. Ophth. **31:** 837 (July) 1948.

Estable concludes that the irritant local effects of drugs on the ocular membranes are studied by direct instillation into the conjunctival sac of one eye of the rabbit, the other eye being treated with isotonic solution of sodium chloride as a control.

The following drugs were tested, in several concentrations: anthraquinone, arsenic trioxide, chrysarobin, colchicine, emetine, histamine, paraphenylenediamine, podophyllin, quinone, menadione and resorcinol.

The clinical manifestations produced by different concentrations of these drugs are described in detail, and a classification in order of potency and concentration is given.

The relation of solubility, physical state, concentration, time of contact and frequency of application of the drugs and their irritant effect is discussed, as are the immediate, acute and delayed inflammatory changes and the opacity of the cornea and its vascularization.

W. S. REESE.

INTRAVITREOUS STREPTOMYCIN: ITS TOXICITY AND DIFFUSION. P. A. GARDINER, I. C. MICHAELSON, R. J. W. REES and J. M. ROBSON, Brit. J. Ophth. **32:** 449 (Aug.) 1948.

The authors describe the methods employed in animal experimentation. Intravitreous injection of 2,000 micrograms of streptomycin acts as a depot from which streptomycin diffuses slowly, chemotherapeutic concentrations still being present in the ocular fluids after three days. The toxic effects of streptomycin introduced into the vitreous in doses of 1.2 and 3.0 mg. result in serious retinal damage. The authors state that these observations are at variance with those of Bellows and associates, who showed that intravitreous injection of streptomycin in amounts of 25 to 1,000 micrograms per dose failed to produce any permanent damage to the fundus. The difference between these results may well be due to differences in the toxicity of the streptomycin used, but the data suggest that at present great caution should be used in the intravitreous use of streptomycin.

W. ZENTMAYER.

Refraction and Accommodation

A SUBJECTIVE PROCEDURE FOR MEASURING AMETROPIA WITHOUT TEST CHART OR GLASSES BY THE USE OF A VARIABLE BAYONET. P. FABRE, Arch. d'opht. **6:** 436, 1946.

After presenting some mathematical considerations, the author proceeds to describe a box which it is possible to rotate on a standard, calibrated to indicate the amount of refractive error by the observation of slits on the screen. The method is reported to be rapid and precise

if the subject possesses good visual acuity. The paper is illustrated, and it should be possible for any one to construct an instrument like the one described.

S. B. MARLOW.

A STUDY OF REFRACTION ACCORDING TO THE TECHNIC USED BY SOME NORTH AMERICAN OPHTHALMOLOGISTS. W. H. CRISP, Bol. Hosp. oftal. Ntra. Sra. de la Luz **3:** 217 (Jan.-Feb.) 1947.

The author states that many ophthalmologists, in their enthusiasm for surgery, neglect the universal importance of refraction. Certain details of technic for the measurement of spherical errors of refraction are mentioned, but the greater part of this paper deals with astigmatism and with methods of examination which are generally not mentioned or are insufficiently described in the textbooks. The author advises the fogging method in examination of patients with hypermetropia. The technic of the use of the crossed cylinder is described in great detail.

M. E. ALVARO.

TOLERANCE OF CONTACT LENSES. S. GYORFFY and A. KAHAN, Ophthalmologica **116:** 1 (July) 1948.

Fifteen persons were tested who complained that they were unable to wear their contact lenses for any useful length of time. Assuming that the contact lens causes irritation of the cornea and conjunctiva, decrease in oxygen metabolism and liberation of histamine, the authors applied a 2 per cent solution of antistin® (2-[N-phenyl-N-benzyl-aminomethyl] imidozotin) and privine® (naphazoline hydrochloride) five minutes prior to wearing the contact lenses. A blanching of the conjunctival vessels resulted, with decrease in corneal sensitivity and no change in the size of the pupil. Nine of the 15 patients tested were able to wear their contact lenses for considerably longer periods after the local application of this drug.

H. P. KIRBER.

Retina and Optic Nerve

CAPILLARY FRAGILITY AND CUTANEOUS LYMPHATIC FLOW IN RELATION TO SYSTEMIC AND RETINAL VASCULAR MANIFESTATIONS: RUTIN THERAPY. J. M. DONEGAN and W. A. THOMAS, Am. J. Ophth. **31:** 671 (June) 1948.

Donegan and Thomas found abnormally increased capillary fragility associated with arteriosclerosis and hypertension, especially in cases of diabetes associated with retinopathy. Rutin decreased the capillary fragility, but not to normal, in cases of diabetes with retinopathy but did not improve vision. It may, however, be significant that there was no loss of vision during a ten to twelve month period of treatment. Rutin appears to be of benefit in cases of Eales's disease and central serous retinopathy.

W. S. REESE.

A CASE OF A GRÖNRLAD-STRANDBERG SYNDROME, WITH DISCIFORM DEGENERATION OF THE MACULAE. G. HIBBERT, Brit. J. Ophth. **32:** 478 (Aug.) 1948.

The patient, a man aged 38, first noticed distortion of objects to his right side. When he was first observed, there were several small ovoid

patches of exudate with faintly pigmented borders scattered throughout the fundus. One year later patches of exudates were present at the macula, and angioid streaks appeared. Changes in the skin appeared during the eighteen months in which the eyes were under observation, though there was a long history of unusual texture of the skin. There was increasing deterioration of vision; when last noted, vision was less than 6/60 in the right eye and 6/24, with eccentric fixation, in the left eye.

W. ZENTMAYER.

HISTOLOGICAL FINDINGS IN A CASE OF ANGIOID STREAKS. F. H. VERHOEFF, Brit. J. Ophth. **32**: 531 (Sept.) 1948.

The eye studied histologically by Verhoeff was from a patient of the late Grady E. Clay, who reported that a few angioid streaks were present in both fundi. The only abnormal histologic changes in the fundus of this eye, aside from the two drusen at the margin of the optic disk, were the basophilia of Bruch's membrane and the gaps in this membrane. The article contains a critical survey of the literature bearing on the histologic features of this condition. The author concludes that angioid streaks result from ruptures of a basophilic Bruch's membrane. The gaps are widened by the elastic tension of the choroid. In the ophthalmoscopic picture, the basophilic condition (calcification) brightens the contiguous fundus and makes conspicuous the dark red choriocapillaris, exposed beneath the pigment epithelium by the ruptures. The streaks are later often altered in appearance by proliferative changes along or within them. The similar ruptures that occasionally occur in senile eyes do not widen into visible streaks, probably because the senile choroid loses its elasticity before Bruch's membrane becomes calcified. Other lesions in the macula and elsewhere in the fundus which are associated with angioid streaks are usually due to proliferative changes involving the pigment epithelium, such as occur under senile degenerative conditions. The subretinal hemorrhages in the macula and elsewhere may be due to ruptures of the choriocapillaris caused by fractures of the calcified membrane. When such a hemorrhage lifts up the pigment epithelium in the macula, "disciform degeneration" results. Hemorrhages arising within the retina are probably explained, as is also circinate retinitis, by the vascular changes that commonly occur in cases of angioid streaks. The association of angioid streaks in many cases with pseudoxanthoma elasticum, in some cases with osteitis deformans (Paget's disease) instead and in still other cases with neither of these conditions is difficult to explain, as is also their association with cardiovascular disease. A possible explanation is that these associations are dependent on hereditary linkages.

W. ZENTMAYER.

MODIFICATIONS IN THE CRITICAL FREQUENCY OF FUSION AFTER SURGICAL REPAIR OF DETACHMENT OF THE RETINA. R. WEEKERS and F. ROUSSEL, Ophthalmologica **115**: 297 (May) 1948.

Operations for detachment of the retina performed within four weeks after the onset will frequently give a perfect result with respect to

visual acuity and field of vision. Measurements of the critical frequency of fusion, however, will show a definite and permanent defect which includes the whole area that was previously detached.

H. P. KIRBER.

Tumors

INTRAEPITHELIAL EPITHELIOMA OF THE CORNEA AND CONJUNCTIVA (BOWEN'S DISEASE). B. ESTERMAN, J. LAVAL and C. OKRAINETZ, Am. J. Ophth. **30:** 1537 (Dec.) 1947.

Esterman, Laval and Okrainetz report a case of Bowen's disease in which cure was apparently effected by radiotherapy without any untoward action on the lens.

W. S. REESE.

MELANOMA OF THE PAPILLA: REPORT OF A CASE. P. SATANOWSKY and P. KURLAT, Arch. de oftal. de Buenos Aires **22:** 141 (July-Aug.) 1947.

A patient aged 46 presented a pigmented tumor on a part of the optic papilla. The growth had not undergone any change over a period of six years of close observation. Visual acuity and the field of vision had remained normal, although for a year and a half the intraocular pressure was increased; this high pressure disappeared with medical treatment.

M. E. ALVARO.

CHONDROSARCOMA OF THE ORBIT. P. SHARKANSKAYA, Vestnik oftal. **25:** 38, 1946.

A man aged 56 noted proptosis of the right eye a few months previously. Examination revealed a firm growth the size of a bean at the upper lateral region of the right orbit. The movement of the eye outward and upward was limited. There was exophthalmos, and funduscopic examination showed papilledema. A malignant growth was suspected (rapid growth of the neoplasm), and an operation was performed. On orbitotomy a tumor was observed outside the muscle funnel; but it could not be removed, so that the Krönlein operation had to be employed. The tumor, the size of a pigeon egg, was excised. After the operation the eyeball collapsed. On the fourth day exophthalmos was still present, with ulceration of the cornea. Within the next two weeks the exophthalmos disappeared and the corneal ulcer healed.

The pathologist made the diagnosis of chondrosarcoma (polymorphism of the cartilage cells and a soft basic substance).

The patient refused to have exenteration of the orbit, and six courses of high voltage roentgen therapy were applied.

Chondrosarcoma is rare; its growth is rather slow, and metastases are not frequent.

O. SITCHEVSKA.

Uvea

VOGT-KOYANAGI SYNDROME. M. PUIG SOLANES, An. Soc. mex. de oftal. y oto-rino-laring. **21:** 12 (Jan.-March) 1947.

The first case was that of a Negro woman aged 25. At the end of two weeks of failing sight, vision in both eyes was blurred. There was a flat detachment of the greater part of both retinas. Eleven days

later there were anterior uveitis and poliosis. She was treated with penicillin and typhoid vaccine. Three months later visual acuity was limited to counting fingers. The condition of the fundus is not stated.

The second case was that of a Negro woman aged 28. Four months before examination, both eyes had become blind within one week. There were precipitates on Descemet's membrane, with posterior synechias. No view of the fundus was obtained. Alopecia developed in the fourth week. The tension increased in both eyes, necessitating scleral diathermy in the left eye. Both eyes were blind.

M. E. Alvaro.

Book Reviews

Report of the Committee on Trachoma of the Second Pan-American Congress of Ophthalmology, Arq. brasil. oftal. **9:** 66-84 (April) 1946.

The president of the Second Pan-American Congress of Ophthalmology appointed a committee on trachoma to collect information on the incidence of trachoma in the Americas. This committee consisted of Dr. Ivo Corrêa Meyer (president), Dr. José A. Senâ, Dr. Jorge Valdeavellano, Dr. Phillips Thygeson and Dr. Polk Richards (who later resigned). This pamphlet is the substance of their report.

In the United States the Indians are believed to have been infected originally by the Spanish invaders, whereas in Canada the Mennonites are considered responsible. Indeed, wherever this sect has settled—whether in Canada or in South America—trachoma has soon become endemic. It seems that they consider the disease a divine punishment, and any attempt to treat it as a flouting of God's will. In the United States, it is estimated that there are 25,000 cases of trachoma among the Indians and 33,000 among other races spread throughout the country.

In Mexico and Central America, Cuba and Haiti, trachoma is not a great problem. In fact, the disease has never been reported in Santo Domingo, Guatemala, Costa Rica, Panama, British Guiana, Jamaica, the Bahamas, Barbados, Bermuda or Trinidad.

Apparently, Brazil is the South American country most afflicted with trachoma. The problem is indeed serious, as large numbers in the states of São Paolo and Rio Grande do Sul are affected. The government is taking energetic prophylactic and curative measures.

In the Argentine, trachoma is endemic in the north, but the capital, Buenos Aires, is free of the disease. Bolivia and Chile have no great problem nor had Paraguay until the Mennonites came. The disease has now followed them into the northern part of that country. The total number of cases in Uruguay is estimated at 1,500. Reports from Peru indicate similar scanty records. Ecuador, Colombia and Venezuela did not answer their questionnaires, but from the national medical literature it appears that the problem of trachoma is not a pressing one.

The contribution ends with the announcement that trachoma is caused by a large virus. The recent therapy with sulfonamide drugs is commented on, in effect, as follows:

"In a disease of chronic evolution, with changeable clinical aspects—latent periods alternating with periods of activity—it is difficult to consider a cure as permanent. The therapeusis, as well as the diagnosis, is made difficult by the doubt concerning the etiology of the disease. One speaks of a clinical diagnosis as one speaks of a clinical cure. It is too early, therefore, to speak of cure of trachoma by the sulfonamide drugs; several more years of experience and observation may be necessary. . . . Up to now all treatments for trachoma have been disagreeable to the patient, being slow and painful. Even were the improvement transitory and the disease only in relapse, there is nevertheless value in the new medicament."

G. M. Bruce.

Le fond d'oeil des hypertendus et des cyanoses. By Daniel Routier. Price, 1,350 fr. Pp. 100, with 232 plates. Paris: Masson et Cie.

The author, who is a cardiologist, has systematically been making an examination of the fundus in all his patients and has taken many photographs of the fundus in black and white with the Nordenson camera. He has collected 232 plates for this study of hypertension and cyanosis. As pictures of the fundus usually show the advanced or rather the terminal, stage the author has studied particularly the preceding conditions, which are more difficult to recognize, and attempts to show how the smallest vessels are affected in hypertensive conditions. The photographs have not been retouched, and each photograph is accompanied with a concise and exact commentary on the general and fundus conditions. The photographs on the whole are successful, although in some the absence of color is noticeable. An accompanying text discusses the changes in turn and, with the illustrations, explains each condition from a physiopathologic standpoint.

After a description of the normal fundus and certain changes which are not pathologic, such as opaque nerve fibers, astigmatism and myopic conus, the author proceeds to a consideration of the eyeground in hypertension. The anomalies in hypertension are grouped as follows: (1) vascular changes: tortuosities, increased reflex streak, venous compression, variation in caliber; localized spasm or generalized contracted arteries; (2) papilloretinal changes: retinal edema, juxtapapillary, perivascular; papillary edema, hemorrhages, exudates.

In one sixth of the cases no change in the fundus was present. While the author subscribes to the great value that ophthalmoscopy occupies in cases of hypertension, he places it between roentgenography and electrocardiography in order of importance as a method of examination.

In the chapter on "Interpretations of Symptoms," the author speaks of how complex are the factors which, on the one hand, cause the anatomic and functional changes in the vessels and, on the other, are followed by all the retinal lesions with which these changes are allied: edema, hemorrhages and exudates. He concludes with the statement that the ocular findings in hypertension are of prognostic value: If they are single, they signify the organic involvement of the arterial system; if multiple and advanced, they announce the serious stage of a fatal outcome. In a concluding chapter he discusses cyanosis.

Dr. Routier is to be congratulated on the publication of this excellent atlas dealing with an important branch of medical ophthalmology. He has taken advantage of modern fundus photography to illustrate his admirable description of the retinal changes observed in hypertension. The atlas shows how valuable is the information obtained by an ophthalmoscopic examination, and the book should be of great interest to the internist, as well as to the ophthalmologist.

ARNOLD KNAPP.

Modern Trends in Ophthalmology. Volume 2. Edited by Arnold Sorsby, M.D. Price, $12.50. Pp. 600, with 169 illustrations and 3 color plates. London: Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1947.

Dr. Arnold Sorsby, the editor of volume 2 of this important series, has corrected certain gaps which were discovered in the contents of volume 1 (reviewed in the ARCHIVES **24**: 426 [Aug.] 1940) and has

made some necessary revisions. A perusal of the table of contents will show how important these new chapters are. The forty-eight subjects are grouped in five sections: physiology, diagnostic procedures, pathology, treatment and social aspects.

The headings of a few of the chapters indicate the broad scope of the book: "Illumination," W. R. Stevens; "The Electrophysiology of the Retina," Ragnar Granit; "Senescence of the Eye," F. P. Fischer; "Gonioscopy," Manuel Uribe Troncoso; "Opthalmodynamometry and Some of Its Clinical Applications," C. Espildora-Luque; "The Nature of Sporadic Congenital Malformations," Ida Mann; "Ocular Manifestations of Vitamin Deficiencies," G. B. Bietti; "Focal Infections," Alan C. Woods; "Virus Affections of the Eye," Arnold Sorsby; "Some Newly Defined Clinical Entities Affecting the Conjunctiva," Phillips Thygeson; "Affections of the Retinal Veins," A. J. Ballantyne; "Lesions of the Retina and Optic Nerve in Association with Blood Dyscrasias," Henry P. Wagener; "Radiotherapy in Ophthalmology," H. B. Stallard; "Sulphonamide Therapy," Arnold Sorsby; "Penicillin," Arnold Sorsby; "Some Problems of Industrial Ophthalmology," Dorothy Adams Campbell, and "Some Ocular Aspects of Aviation," P. C. Livingston.

The 169 illustrations and 3 color plates are excellent, and the guiding bibliographies add to the usefulness of the volume.

The purpose of the book is a happy one and cannot fail to be of great value and interest to all ophthalmologists.

ARNOLD KNAPP.

Cybernetics, or Control and Communication in the Animal and the Machine. By Norbert Wiener. Price, $3. Pp. 189. New York: John Wiley & Sons, Inc., 1948.

This is an extremely thought-provoking book, by the professor of mathematics of the Masachusetts Institute of Technology. The subject matter ranges from mathematical calculators to the nerves and brain of the human body. It is the outcome of a monthly series of discussion meetings, the participants of which were mostly young scientists at the Harvard Medical School who gathered for dinner about a round table in Vanderbilt Hall. At each meeting, one of the group or an invited guest would read a paper on some scientific topic, generally one in which methods of methodology were the first consideration. General discussion followed, and the meetings were apparently not for those who were unable to stand frank criticism. The author, whose field is mathematics, was therefore exposed to experts in many different fields of biology and medicine. He soon became aware that there were common grounds and that the problems of one science might be solved, or at least simplified, by the solutions found in others. This book is an attempt to explain the physiology of parts of the nervous system on the engineering principles and mathematics employed in the development of calculating machines or automatic pilots, or the general principle of what are called "feed backs."

While most of the book is undoubtedly far beyond the ken of most mortals, the chapters "Computing Machines and the Nervous System," "Gestalt and Universals" and "Cybernetics and Psychopathology" are extremely interesting; and where the author descends to what he admits is probably an oversimplification of the picture, one gets a pretty good

idea of how a visual organ may function. While the book has no practical value for the ophthalmologist, it is well worth while for those who like to explore the upper ether.

FRANCIS H. ADLER, M.D.

Diseases of the Fundus Oculi with Atlas. By Adalbert Fuchs, M.D., E. O. Professor of Ophthalmology of the University of Vienna. First English Edition. Translated by Eric Pressburger, M.D.; Edited by Abraham Schlossman, M.D. Philadelphia: The Blakiston Company, 1949. Edition limited to 995 numbered copies.

This beautifully illustrated text on diseases of the ocular fundus is the first English edition of the author's well known book in German. It is greatly to the credit of the American publishers that they have undertaken this edition, which is limited to slightly less than 1,000 copies. The text has exceptional value because of the author's long experience in the histopathology of the eye. As a result of this, he is able to correlate the ophthalmoscopically visible changes with the histologic picture, and a unique feature of the book is the publication of plates illustrating the histopathology along with the fundus picture.

The translation by Dr. Eric Pressburger is excellent and, unlike so many translations, particularly those from the German, is in good English style with short, readable sentences. Some of this credit must also go to the editor, Dr. Abraham Schlossman.

The book is divided into the usual sections on the appearance of the normal fundus, congenital anomalies and, then, diseases of the various anatomic parts of the eye, such as the optic nerve, retina and choroid. Special chapters on certain diseases of the eye, such as glaucoma, tuberculosis, syphilis, tumors and detachment of the retina, follow.

While the plates are not as good as those in the early German and English atlases, they are the best which have appeared in recent years in any language, particularly in English. In spite of its cost, this book should be bought by all who have a serious interest in the ophthalmoscopic changes in local and general diseases.

FRANCIS H. ADLER.

Gonioscopy. By Dr. Jules François. Price not stated. Pp. 233, with 156 figures, 48 in color. Louvain, Belgium: Librairie R. Fonteyn, 1948.

This book was commissioned by the Belgian Ophthalmological Society and is an excellent review of what is known of the filtration angle in the normal human subject and in the various forms of glaucoma. It is written in French, but contains an excellent bibliography of the world's literature. It is of interest to note that the majority of these references are to authors in this country.

The first chapter deals with the anatomy of the normal angle. In the next chapter, the importance of the canal of Schlemm is considered, and various theories on the outflow of aqueous are enumerated. There is a good section on the aqueous veins. Noticeable for its absence is any reference to the work of Friedenwald, who, it will be remembered, was the first investigator to find efferent arteries to the canal of Schlemm. Chapter 3 deals with the technic of gonioscopy and chapter 4 with the normal aspects of the angle. Chapter 5 is concerned with congenital

anomalies of the anterior segment of the eye and chapter 6 with traumatic lesions of the angle. Tumors of the angle are considered in chapter 7, and the author devotes chapter 8 to a consideration of anterior synechias, which he terms *goniosynechies*. Following this is a chapter on the information derived from gonioscopy in cases of iridocyclitis and uveitis. Chapter 10 deals with gonioscopy of primary simple glaucoma, chapter 11 with secondary glaucoma and chapter 12 with the gonioscopic appearance of the angle postoperatively.

Although in French, the author's style is easy, and the book is excellently documented with illustrations. It is a worthy minor companion to Troncoso's authoritative book.

FRANCIS HEED ADLER.

Handbook of Ophthalmology. By Everett L. Goar, Professor of Ophthalmology, Baylor University College of Medicine, Houston, Texas. Price, $5.50. Pp. 166, with 48 illustrations in text and 7 color plates. St. Louis: C. V. Mosby Co., 1948.

Goar believes that the ophthalmologic books available to the junior medical student, who ordinarily has about a dozen other subjects to occupy his attention, are too complete. The same opinion has long been held by O'Brien (O'Brien, C. S.: Ophthalmologic Notes for Students, Iowa City, Athens Press, 1930, p. 370) and others. Dr. Goar's lectures on ophthalmology have been illustrated and slightly expanded into this volume, which is frankly designed for the use of medical students.

The subject matter follows the conventional lines of similar textbooks and is covered in chapters on anatomy, physiology, embryology, methods of examination, refraction and diseases of the various structures, in anatomic order.

If one accepts Dr. Goar's thesis (and it certainly has merit) that such books as May's and Gifford's contain too much material, this volume should prove of great time-saving value to the medical student and should enable him to pass his examinations. He will not, of course, be exposed to as much ophthalmology as if he were to study the older texts, but he always has them available if he wishes to pursue the subject further. Dr. Goar has modestly suggested that the book is intended for students only, but it should prove a valuable guide to any teacher faced with the task of organizing, or reorganizing, a course in ophthalmology. It speaks well for the teaching of this specialty at Baylor University.

G. M. BRUCE.

The Anatomy of the Eye and Orbit. Third Edition. By Eugene Wolff. M.B., B.S., F.R.C.S. Price, $12. Pp. 440, with 323 illustrations, 24 in color. Philadelphia: The Blakiston Company, 1948.

More than eighty illustrations have been added to the third, and revised, edition of this popular anatomy. The majority of the illustrations were prepared from sections made in the pathologic laboratory of what is now the Westminster branch of the combined Royal and Westminster hospitals. The main changes in the text are in the description of the ciliary muscle, the substantia propria of the cornea, the vitreous, the zonule of Zinn, the distribution of the lacrimal fluid, the mucocutaneous junction of the lid margin, the precorneal film, the retinal capillaries and the central connections of the visual apparatus.

The illustrations number 323, including 24 in color; these, in their clearness and selections, constitute a most important part, which with the excellence of the text, make this an important and essential book for study and reference. Though the book has been previously reviewed (ARCH. OPHTH. **25:** 526 [March] 1941), it may not be amiss again to draw attention to a few headings in the contents: "The Visual Pathway," "The Involuntary Nervous System," "The Path of the Light Reflex," "The Development of the Eye" and "Comparative Anatomy."

The completeness, the clearness of the text, with its many practical clinical comments, and the excellence of the illustrations make this a thoroughly practical textbook, which deserves continuity of its popularity.

ARNOLD KNAPP.

Year Book of Eye, Ear, Nose and Throat. Edited by Louis Bothman, M.D. and Samuel J. Crowe, M.D. Price, $4.75. Pp. 511. Chicago: The Year Book Publishers, Inc., 1948.

This year's Year Book brings again in a compact and handy form an accurate review of the past year's publications in ophthalmology. The subject of the special article written by the ophthalmologic editor, Dr. Louis Bothman, is: "When Should Cataracts Be Operated On?" The abstracts, as usual, are classified on an anatomic basic, and there are several special chapters. The one on glaucoma includes a long review of Dr. Magitot's article on the "Intracranial Origin of Glaucomatous Optic Atrophy"; in the chapter on neurology and visual fields there is a review of Dr. M. Amsler's article on "Qualitative Examination of Macular Function"; the chapter on therapy is particularly complete and even reviews an article by M. Toulant on "Tissue Therapy in Ophthalmology"; the chapter on surgery, which comprises 43 pages of the 233 pages devoted to the eye in this Year Book, illustrates the interest that the surgical part of ophthalmic practice now possesses. An index of subject matter and authors' names conclude the volume. The abstract titles are complete and the abstracting is excellently done, while the author's frequent comments are valuable.

This is a useful compendium, which can be confidently recommended to every practicing ophthalmologist.

ARNOLD KNAPP.

Some Aspects of Oculo-Refractive Technique. By Malcolm Cholerton. Price 21s. Pp. 144, with 23 illustrations. London, England: Hammond, Hammond, Hammond & Company, Ltd., 1948.

In the preface, the author states that this book is "an outline of the field study which engages the ophthalmic optician." The style in which it is written assumes a fair knowledge of the subject. The style is reminiscent of Chavasse and will not be easy reading for the novice.

Although the book purports to be a compendium covering the whole field of refraction and ocular muscle imbalances in 144 pages, the author spends much valuable space on subjects of little practical importance, such as aniseikonia and dynamic retinoscopy. It is hard to see how it can be of any value to an ophthalmologist.

FRANCIS H. ADLER.

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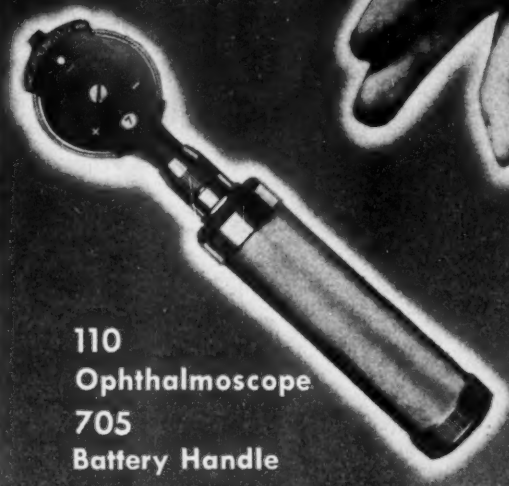

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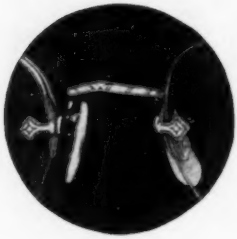

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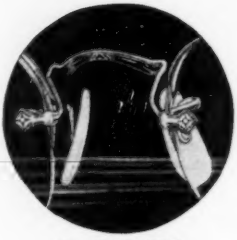

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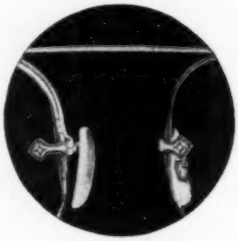

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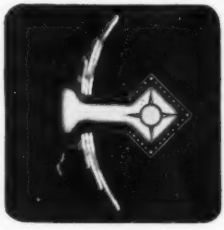

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by Thurman B. Rice, M.D.

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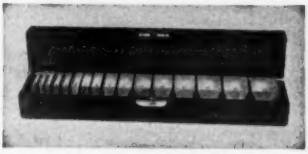

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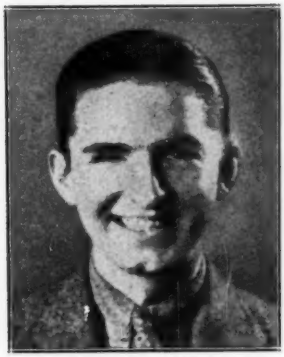

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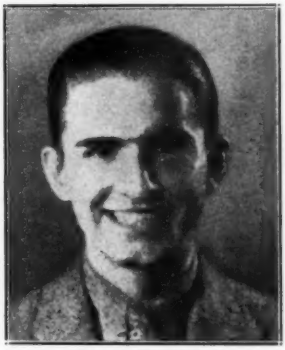

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